首届中英肿瘤论坛
暨肿瘤转移基础与临床研究论坛
China-United Kingdom Cancer Conference 2014，CUKC 2014
2014・北京/Beijing

会议手册
Conference Brochure

主办单位
Major Organizers
首都医科大学
Capital Medical University
卡迪夫大学
Cardiff University

承办单位
Organizers
首都医科大学肿瘤研究所
Cancer Institute, CMU
首都医科大学肺癌诊疗中心
Beijing Lung Cancer Centre, CMU
首都医科大学普通外科学系
Department of General Surgery, CMU
首都医科大学肿瘤学系
Department of Oncology, CMU
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尊敬的各位来宾，各位代表，各位朋友：

中国有句古话叫：“有朋自远方来，不亦乐乎？在总理李克强先生刚刚对英国成功访问不到两周，今天我们迎来了远在英国的大学的15名同道来参加首届中英肿瘤论坛。同时，学校内近200位专家学者也参加了本次论坛。值得高兴的是，长期以来关注首医科大学发展并为此做出突出贡献的学者也莅临报告。更值得高兴的是，北京市教委、科委、卫计委和卫生局等相关部门也莅临论坛开幕式。在这一值得纪念的日子里，请允许我代表首医科大学对家内外嘉宾参加本次论坛，对两位院士的莅临并做主旨报告，对首都各界领导对我校持续不断的指导与支持表示深深地感谢。

2007年，大学与首医科大学首钢建立校际合作协议，之后，在David Grant校长，Prof. Colin Riordan校长的积极倡导下，两校青年学者交流不断增加，迄今已有50多位中国学者和30多位首医科大学的学生在卡迪夫大学留学研究，双方共同签署了一份与肿瘤学相关的合作论文50余篇，去年有两位卡迪夫大学的学生到我校进修1个月，2013年10月28日，两校签署了“医学教育合作协议”，标志着双方的合作关系进入到一个新的阶段。今天，卡迪夫的新的中国医学奖学金项目正式启动，相信这一奖学金能帮助更多中国学生实现交流互访。在英国，我校派往卡迪夫大学基础医学专业的7名本科生将首次启程，他们将在贵校科研实习6个月，开启了两校本科生交流的先河。而明年，我们也期待着卡迪夫大学学生能继续在我校实习。

Respected guests, colleagues and friends,

For thousands of years, we Chinese have proud to use the phrase 'What a pleasure to have friends come from afar!'. Just two weeks ago, the Chinese Prime Minister Li Keqiang successful visited the UK, today, it is our great pleasure in welcoming the delegate of Cardiff University UK to participate the China-UK Cancer Conference 2014. Likewise, it is my pleasure in welcoming over 200 home colleagues in participating the conference. I wish to extend a special welcome to Academician Cheng Shujun and Academician Wu Yiling, who have made enormous contribution to cancer in China and to the development of Capital Medical University. I am very grateful for the officials from the Commissions of Education, Science, Health and Hospital Authority of the Government in attending today's opening ceremony. I wish to take the opportunity to welcome you all, colleagues home and abroad, governmental officials to the conference and thank you all for supporting the CMU over the years!

In 2007, Cardiff University and Capital Medical University entered a formal link after signing the agreement of collaboration. Subsequently supported by the successive Vice-Chancellors, Dr David Grant and Colin Riordan, there have been a rapid expansion in our collaborations in research and scholar exchanges. More than fifty medical scholars and more than 30 CMU students have gone to Cardiff to study and carry out research. They have had a series of joint discoveries and publications. CMU have also hosted undergraduates and postgraduates from Cardiff in the past years. In October 2013, Cardiff and Capital Medical University have entered a new stage of relationship after signing a comprehensive agreement in education. It is very pleasing in noting the launch of the new Phase of Cardiff's China Medical Scholarship, which I trust will allow more medical scholars and medical scientists to study and exchange with Cardiff and the UK. In little
These case examples clearly demonstrate the benefits of opening, improving, and expanding medical education in China. This has come with the establishment of medical universities and research institutions, which have significantly contributed to the development of medical science and technology.

Of course, there are challenges and problems we need to address. For example, the overall medical care infrastructure in China is not as advanced as it is in many Western countries. This includes issues such as healthcare access, medical education, and research. Nevertheless, with the support of international collaboration and cooperation, we can overcome these challenges.

I congratulate the opening of the China-UK Cancer Conference and hope it is not only an academic platform, it is also a venue for new ideas and new collaboration. China has evolved in economy, science, research and in almost every aspect of life over the past forty years. I hope our UK and home friends also have the opportunity to visit China and enjoy the hospitality of which we are always proud.

Thank you all.

Professor Lu Zhaozhen
President of Capital Medical University
Dear distinguished guests, friends, colleagues, ladies and gentlemen,

On behalf of Cardiff University, and together with co-host Capital Medical University, I wish to extend a very warm welcome to you all to the China-UK Cancer Conference 2014, here in the beautiful and historical city of Beijing.

Cardiff is honoured to host this important international conference with our long-term partner, Capital Medical University. With an ever-increasing life expectancy and a broad number of social and environmental reasons, cancer has become the leading cause of death in the UK, in China and indeed the world. It has resulted in many lives being lost and it has become the biggest burden to the healthcare system so it continues to pose challenges for patients, the medical community and society as a whole. The world has realised the importance of joint efforts in finding a cure for this disease. The collaboration between China and UK serves a good example of these efforts.

Cardiff has enjoyed a long relationship with China spanning decades. However, the past decade has witnessed a greater effort in the development of collaboration in the fight against cancer, in research, in education, in healthcare and indeed in other health and social related sections in cancer care. Cardiff has particularly enjoyed our strong partnership with our co-host, Capital Medical University, Peking University and other organisations such as the Yiling Group, which covers broad areas of research, R&D to medicines and healthcare. The Cardiff-CMU/China links have resulted in some fruitful outcomes, from student/scientist exchanges, joint research publications, new diagnosis,
to new medicines. Cardiff is pleased with the formation of the Joint Research Centre with CMU and proud of its highly successful China Medical Scholarship. Our success is now recognised by several awards including the China-UK Cancer Research International Base (Beijing), the Key Laboratories of Cancer Metastasis by the Beijing Government and of course by the TIMES Higher Education International Collaboration of the Year award. This illustrates Cardiff’s international mission in China. Cardiff is at the very heart of the China-UK collaborations and is a ‘shining example of the Sino-UK scientific collaboration’, a remark made by Madam MeiYing Zhang, the Vice-Chairman of the CPPCC of China. According to British Ambassador to China, Sebastian Wood CMG, ”I am delighted that Cardiff is opening a new biomedical research centre with Capital Medical University. This is a great example of the long term commitment of the UK’s leading universities to work in collaboration with their Chinese counterparts.”

Looking ahead, Cardiff has ambitious plans in research collaboration in cancer, medicine and other areas with China and will endeavour to work with our Chinese partners in the battle against cancer.

I hope you all enjoy this exciting conference and wish everyone every success with the CUKC 2014. CUKC 2015 will be held in Cardiff, when we’ll warmly welcome our Chinese partners and colleagues to come to the event and enjoy beautiful Wales and United Kingdom.

Hywel Thomas 教授
英国皇家学会院士
卡迪夫大学副校长
论坛组织结构
(Origansng Committees)

名誉顾问 (Honorary Consultant):

程书钧 院士 (Academician Cheng Shujun)

论坛主席 (Conference Chairmen):

吕兆丰 (Lu Zhao Feng) 、Hywel Thomas

论坛副主席 (Conference Vice-Chairmen):

王晓民 (Wang Xiaomin)  姜文国 (Wen G. Jiang)

执行主席 (Executives):

安 威 (An Wei) 、支修益 (Zhi Xiuyi) 、张忠涛 (Zhang Zhongtao) 、任 军 (Ren Jun)

秘书长 (Conference Secretary):

张玉祥 (Zhang Yuxiang)

论坛秘书 (Conference secretariat):

李 杨 (Li Yang) 、杨晓梅 (Yang Xiaomei) 、司 杨 (Si Yang) 、白志刚 (Bai Zhigang) 、胡 牧 (Hu Mu)

余和芬 (Yu Hefen) 、程 杉 (Cheng Shan) 、滕 旭 (Teng Xu)
The Capital Medical University (CMU) was founded in 1960. It ranks amongst the top medical institutions in China and is one of the key municipal universities in Beijing. Professor Wu Jieping, a well-known urologist and an academician of the Chinese Academy of Sciences and the Chinese Academy of Engineering as well, was the founder of CMU. The current president of CMU is professor Lu Zhaofeng.

CMU consists of 10 schools, 19 affiliated hospitals
医院（第九临床医学院）、附属北京胸科医院（第十临床医学院）、北京三博脑科医院（第十一临床医学院）、附属北京地坛医院（第十二临床医学院）、附属北京儿童医院（儿科医学院）、附属北京口腔医院（口腔医学院）、附属北京安定医院（精神卫生学院）、附属北京妇产医院（妇产医学院）、附属北京中医医院（中医药临床医学院）、附属北京世纪坛医院（肿瘤医学部）、中国康复研究中心（康复医学院）和附属北京康复医院（北京康复医学部）。以及预防医学教育基地（北京市疾病预防控制中心）。

学校还设有37个临床专科学院，临床学系。

学校学科力量雄厚。现有8个国家重点学科，2个国家重点（培育）学科，56个国家临床重点专科（含中医），14个国家中医药管理局重点（培育）学科，4个北京市一级重点学科，6个北京市二级重点学科，1个北京市重点交叉学科，2个北京市一级重点建设学科，6个北京市二级重点建设学科，1个北京市重点学科群。3个国家临床医学研究中心，1个省级研究基地，1个省级研究基地，3个教育部重点实验室，1个教育部部实验室，1个教育部部实验室，1个教育部部实验室，1个教育部部实验室，1个教育部部实验室。有8个一级学科博士学位授权点和11个一级学科硕士学位授权点；按照三级学科统计，有59个硕士学位授权点和78个硕士学位授权点，有9个博士后科研流动站。

学校本专科专业齐全，设置的七年制专业中有临床医学（包括儿科方向）和口腔医学；本科专业中有临床医学、基础医学、口腔医学、预防医学、药学、中医学、中药学、护理学、生物医学工程、康复治疗学、公共事业管理（卫生管理）、医学实验技术、法学（卫生法学）、临床药学、医学检验技术等16个专业。高职高专教育设有护理、医学检验技术、药学等14个专业。现有全日制在校生10132人，其中研究生2943人，长学制学生1559人，本科学生3214人，高职生1983人，留学生433人；成教生4654人。学校

and 1 teaching institution. The university has about 35,128 faculties and staffs. Among the staffs, there are 6 academicians of the Chinese Academy of Sciences or the Chinese Academy of Engineering. The university has 1,875 full-professors, and 3,275 associate professors.

Annually, there are ca. 2,000 students enrolled in CMU and at present, a total of 10,132 students are studying in this university. The university provides a diverse spectrum of programs for undergraduate, master degree, doctoral degree and other medicine-related programs to meet a variety of students’ requirements.

The university hospital offers a great amounts of programs for training thousands of clinical residents and fellows annually. In addition, the faculty members provide continuous medical education
培养医学与医学相关学科的学术型和应用型人才，形成了全方位、多层次、创新型人才培养模式。

学校目前有教育部、卫生计生委“卓越医生教育培养计划”试点项目4个，7个国家级特色专业和10个北京市级特色专业，7门国家级精品课程和18门市级精品课程，2个国家级实验教学示范中心和5个市级实验教学示范中心，3个国家级人才培养模式创新实验区和1个市级人才培养模式创新实验区，1个国家级大学生校外实践教育基地，4个北京市级校外人才培养基地和1个素质教育基地，7个国家级优秀教学团队和11个市级优秀教学团队，1名国家级教学名师和16名市级教学名师。通过教育教学改革实践，近五年学校获得教育教学成果国家级特等奖1项、二等奖2项；北京市特等奖1项、一等奖6项、二等奖10项。

学校具有较强的教学发展与科研实力，在校本部和附属医院拥有一批国家级和市级重点学科和重点实验室的基础上，建有高水平的国家级、市级研究和培训机构，如国家医学检验与技术人才培养基地、卫生部全科医学培训中心、北京市全科医学培训中心、首都卫生管理与政策研究基地等。有1个国家工程技术研究中心、4个教育部工程研究中心、7个北京市工程技术研究中心。近5年来，学校承担了国家“973”、“863”、国家自然科学基金、国家社会科学基金、北京市自然科学基金，以及国家教育部、卫生计生委、科技部、北京市科委、北京市教委等科研项目2319项（其中国家级科研项目1137项），累计科研经费16.9亿元；获得各类各级奖励84项，其中国家级科技进步奖8项，北京市科技奖29项、教育部高等学校科学研究优秀成果奖21项、中华医学科技奖20项、何梁何利科学与技术进步奖1项、吴阶平医学奖3项、北京市哲学社会科学优秀成果奖2项；获得专利授权297项。神经生物学、细胞生物学、基础免疫学、医学图像处理、生物信息检测与处理、神经内科、神经外科、

(CME) for physicians and other health professionals through seminars, teaching rounds, tutorials and webinars on and off the campuses. Over the years, many graduates of the university have become academic leaders and famous general practitioners in Beijing and around the whole country.

CMU is also an academic institution with proud of its strong competence in scientific research. It hosts many the municipal/national key laboratories and disciplines. A plenty of national research and training centers are located in the university, such as the general pratice training center, the clinical engineering training center, the center for traditional chinese medicine and so on. CMU is acknowleged for its academic performance.
in many disciplines or subjects such as neurobiology, infection and immunity, medical imaging, neurology, neurosurgery, cardiology, cardiovascular surgery, organ transplantation, respiratory and digestive disease, oral-maxillofacial surgery, ophthalmology, otolaryngology and pediatric hematology.

CMU has established a number of international exchange programs including faculty and student exchange. The collaboration partners of this university include many well-recognized institutions across the world. CMU is proud to be at the forefront in the medical education, biomedical research and patient care. It is committed to bringing the latest knowledge in basic and clinical sciences to fuel the transformation of health care.
了友好交流合作协定。先后接待50多个国家和地区的专家学者和学生数百人来校进行学术交流和参观访问。目前，我校聘请的外籍专家共24人，聘请的外国及港澳台地区客座教授67人；在校学历教育海外学生467名，覆盖40多个国家和地区。学校海外学生涵盖了本科、硕士、博士研究生及进修生。同时，学校积极选送教师、科研人员和管理干部出国进修，参加学术会议和考察访问。

建校50多年来，学校形成了“扶伤济世、敬德修业”的校训、“爱国奉献、艰苦奋斗、救死扶伤、严谨求实”的校风和“勤学、博思、求精、创新”的学风，并形成了比较完整的学校文化标识系统。同时，不断以首医人的奋斗历程丰富着“首医精神”的文化宝库，激励着首医人继续团结奋进。

校党委始终把加强党的先进性建设、推动事业科学发展作为学校党建和思想政治工作的根本出发点和落脚点，“在冲锋中建先锋”的党建理念深入人心。学校坚持育人为本、德育为先，不断加强学生德育和教育管理工作。2007年，学校获评北京市党建和思想政治工作先进高校。

全体首医人求真务实、齐心协力、自主创新、和谐发展，正在努力将首都医科大学建设成为立足首都、面向全国、走向世界、国内一流、国际知名的医科大学。
Cardiff University is a world-leading, research excellent, educationally outstanding university, driven by creativity and curiosity. We are a member of the UK’s “Ivy League” of Russell Group research intensive universities. Our global community, reputation and partnerships are at the centre of our identity. Our collaborative work with academic partners across the world produces research with real impact. Examples include collaborations with researchers in China to tackle breast cancer or studying the genetics and demographics of mammals in our field centre in Borneo.

Across the Institution we have formal links with more than 35 countries including 38 partnerships with China, 16 in the US and 12 with Malaysia. We are partners with ‘Santander Universities’ and the Fulbright and Marshall Commissions, allowing for teaching and other
collaborations to flourish with North and South America. Our thriving international student community of more than 3,700 students from 100 different countries plays a very significant role in the international life of our institution and across Wales. A growing number of our students undertake a period of study overseas annually as part of their degree. This helps them build cultural awareness and enhance their employability. We also welcome hundreds of students from continental Europe and further afield on exchange programmes. We have more than 170,000 alumni in over 170 countries around the world. Our graduates return home as ambassadors for Cardiff University, Wales and the UK and often play an important role in developing good diplomatic and trade relations. We also attract the highest calibre of researchers from around the world who further enhance the learning experience for students.
The Cancer Institute of Capital Medical University was formed in 2011, when Professor Hongti Jia became the first director. Since 2013, Professor Wen Guo Jiang has been the director of the Institute. The Cancer Institute aims to integrate the basic, translational and clinical cancer resources of Capital Medical University and establish a cancer research organisation with full integration between basic research and clinical practice. The Cancer Institute is supported by a strong academic advisory board which is formed by renowned scientists including 5 academicians and a Noble Prize winner for medicine. Capital Medical University has some outstanding clinical resources. The Institute has pooled all research leaders, research groups and disciplines in the area of cancer and cancer research within Capital Medical University. Together with central and analytical services, clinical leaders and groups in the area of clinical oncology, the intention is to create a multiple disciplinary, integrated cancer research team.

Capital Medical University and the Cancer Institute have long standing international collaborations. Notably, it has formed the Capital Medical University-Cardiff University Joint Centre for Biomedical Research, the China-UK Cancer Research International Collaboration Base (Beijing) and the Cancer Invasion and Metastasis Key Laboratory (Beijing).

The Institute follows a principle of innovation, integration and collaboration and aims to make significant advances in the areas of cancer invasion and metastasis, biomarkers and translational cancer research.
首都医科大学肺癌诊疗中心
The Lung Cancer Center Captiral Medical University

首都医科大学肺癌诊疗中心成立于 2003 年 4 月。宣武医院胸外科主任张教授担任肺癌中心主任。首都医科大学肺癌诊疗中心在历任学校领导的大力支持下，整合首都医科大学各附属教学医院胸外科、呼吸科、肿瘤科、放疗科、病理科和医学影像学科等肺癌诊疗领域的相关学科资源，构建了一个多中心多学科协作的临床研究平台。

首都医科大学肺癌诊疗中心专家顾问包括中国胸外科领域黄国俊、辛育龄、赵志军、李泽坚和鹿宗俊教授，我国肿瘤学界孙燕院士和程书钧院士，中国科学院学部委员、中国血液学研究所主任陈子介教授、美国胸外科专家 David Jablons 教授、美国 M.D.Anderson 癌症中心肺科专家 Mao Lee 教授和英国卡迪夫大学姜文国教授。

首都医科大学肺癌诊疗中心成立 11 年来，举办各种有关肺癌防治的学术交流和科普宣传活动百十余场，成功策划并主持召开第 1-6 届中国肺癌南北高峰论坛、第 1-5 届中日韩肺癌专题研讨会、第 1-8 届

The Lung Cancer Center Capital Medical University was established in April 2003, headed by Professor Xiuyi Zhi from the Thoracic Surgery Department Xuanwu Hospital. The Lung Cancer Center, which was strongly supported by school leader of Capital Medical University integrated thoracic surgery, respiratory, oncology, radiotherapy, pathology and other related disciplines of lung cancer treatment among every Capital Medical University affiliated teaching hospital and built a multi-center clinical research platform of multidisciplinary collaboration.

The Lung Cancer Center awarded consultants include Professors Guojun Huang, Yuling Xin, Zhiwen Zhao, Zejian Li, Zongjun Dong of Chinese Thoracic Surgery and academicians of oncology Professor Yan Sun and Professor Shijun Cheng, Professor Jin Su Lee from Korea’s National Cancer Center, Professor Jin Su Lee from Japan’s National Cancer Center, together with professor David Jablons from the University of California, Professor Mao Lee from the MD Anderson Cancer Center and Professor Wenguo Jiang from Cardiff University.
During the 11 year history of the Lung Cancer Center, we have held various academic exchanges on tobacco control, lung cancer prevention and scientific activities, including the 1st-6th of China’s North and South Lung Cancer Summit, the 1st-5th Sino-Japan-Korea Joint Lung Cancer Symposium, the 1st-8th Director of the China Thoracic Surgery Peak Forum and the 1st-3rd China Tobacco Control and Lung Cancer Prevention Forum. For ten consecutive years the Lung Cancer Center has held the national new technology and new progress in lung cancer diagnosis and treatment course (continue education program at the national level CME).

The Lung Cancer Center Capital Medical University has established excellent relations with domestic, and foreign lung cancer centers and lung cancer research institutes. Professor Xiuyi Zhi and Professor David Jablons developed the China and the United States Lung Cancer Clinical Trials Union (CCTC) and with Professor Wenguo Jiang from Cardiff University, established the Chinese-UK Lung Cancer Laboratory.

The Lung Cancer Center carried out two CCTC clinical research projects with the results being published in both The Lancet and the Journal of Thoracic Disease. Our center has also undertaken the Beijing Natural Fund, Capital Medical Development Funds, Capital Medical Major Research Projects, the Beijing Municipal Science and Technology Commission Projects and the Wu Jieping Medicine Prize Foundation Research Project. The Lung Cancer Center will continue its collaborations with Capital Medical University, the Capital Medical University Cancer Institute and the Department of Tumours to build a major lung cancer tissue bank and database and carry out international cooperation dedicated to medical research.
The Digestive Oncology Research Center of the Cancer Institute, Capital Medical University, has integrated the resources of digestive system cancers, clinical and basic research, within Capital Medical University. It emphasises a bed to bench and bench to bed translation. The main purpose of the Center is to focus on digestive malignancies by acting as a focal point to connect clinicians and research scientists, to improve the quality of research and medical/surgical treatment. The center is composed of the Faculty of General Surgery of Capital Medical University and Biochemistry and Molecular Biology Department of the College of Basic Medicine. The main research directions are the mechanism of gastrointestinal tumour invasion and metastasis and the mechanisms of chemotherapy resistance, tumorigenesis and tumour progression. Currently there are 4 professors and over 10 associate professors in the research center.
Beijing Shijitan Hospital, founded in 1915 and affiliated to Capital Medical University, is one of the most well-established hospitals in Beijing. As Capital Medical University Cancer Center, the Ninth Clinical Medical College of Peking University, the hospital is a tertiary A-level comprehensive hospital and a class A health care hospital. In February, 2012, in conjunction with the national health care reform, the hospital as the core unit, led to form the Shijitan Hospital Medical Complex, consisting of 11 hospitals. There are 1100 beds and over 300 professionals with senior technical titles at the hospital. The hospital grants doctorate and master degree bases for 31 disciplines, and has 12 Beijing municipal bases for residents training.

It has the national key discipline of Traditional Chinese Medicine, Beijing Key Laboratory of Cancer Therapeutic Vaccines, Duke Applied Therapeutics Center-CMU Cancer Center Institute of Cancer Research, and Joint Cancer Translational Research Center with Institute of Basic Medicine, AMMS, Beijing Cancer Institute of Chinese and Western Integrative Medicine, and is also the national drug clinical trial
Center with a well-equipped Phase I trial center.

The key departments are the Cancer Center with an advanced internationalized Cancer Immunotherapy Center, Clinical Laboratory, Cardiology, Vascular Surgery Center and Neurology. Rapidly-developing departments are Gastroenterology, General Surgery, Head and Neck Oncology Surgery, Obstetrics and Gynecology, Respiratory and Orthopedics. The disciplines with their own features are Geriatrics, Neurosurgery, Allergy and Pediatrics. Among them, Ge’s Pinching Sinew and Tapping Manipulation at the Department of Traditional Chinese Orthopedics and Traumatology has been selected as the national intangible cultural heritage.

The Hospital has been continuously looking into the development patterns of “being a larger specialized cancer center and a stronger comprehensive hospital”, with balanced advancement of various disciplines to accomplish the goal of becoming a modern academic brand hospital.
程书钧 院士

著名肿瘤病因学专家，中国工程院（医院）研究员，中国工程院院士。

程书钧院士曾任中国医学科学院肿瘤研究所副所长，肿瘤医院副院长，现任中国医学科学院和协和医科大学学术委员会执行委员，中国环境诱变剂学会理事长，中国抗癌协会副理事长。

程书钧院士先后主持了国家“七五”、“八五”、“九五”肿瘤攻关有关课题研究，建立了有先进水平的致癌动物、致癌物和抗癌药物生物检测系统。早在1987年就在我国建立了可用于人上皮细胞培养的无血清培养基和培养技术，并应用于肿瘤病因和癌变机理研究。他20多年来从事和参与分子机理和肿瘤分子标志谱研究，特别是在天然抗肿瘤物的研究方面取得重要进展，发明绿茶多酚素治疗尖锐湿疣，此项原创发明成果已获国际专利，并在美国FDA申请了新药，2006年经美国FDA批准上市。这是美国50多年来首次批准一个复杂成分的植物药作为处方药上市销售。他现任国家重点基础研究发展规划“973”肿瘤项目和北京市重大肿瘤专项的首席科学家。

程书钧院士曾兼任首都医科大学肿瘤学系主任，首都医科大学肿瘤研究所肿瘤遗传和转移机制研究北京市重点实验室委员会主任。

Professor Cheng Shujun, a well-known cancer researcher and cancer etiologist, is a research fellow at the Cancer Institute & Hospital of Chinese Academy of Medical Sciences, and an academician of the Chinese Academy of Engineering. Academician Cheng served as the Deputy Director of the Cancer Institute & Hospital of Chinese Academy of Medical Sciences between 1992 and 2001. Currently he is an executive member of the Academic Committee in Chinese Academy of Medical Sciences and Peking Union Medical College, the Chairman of Chinese Environmental Mutagen Society, and the Associate Chairman of the Chinese Anti-cancer Association.

Academician Cheng has been awarded several national-level grants such as funding from national "75", "85", "95" five-year plan, and has established the advanced biological systems for testing mutagens, carcinogens. As early as 1987 he established a serum-free culture system which has been used for growing human epithelial cells in order to study the mechanism of carcinogenesis. He has carried out research projects on molecular mechanisms and biomarkers of lung cancer for more than 30 years. Significantly, he has made important advances in natural anti-carcinogen screening research, and discovered that green tea catechins are effective for the treatment of Genital Warts caused by the human papilloma virus (HPV), which has been approved for international patent application. This special extract of green tea has been approved as a new prescription drug by the United States FDA in 2006. This is the first time for the United States to approve a complex composition of herbal medicine as a prescription drug in more than 50 years.

Academician Cheng currently also serves as Chairman of the Department of Medical Oncology, Capital Medical University, and the Academic Committee of Beijing Key Laboratory for Cancer Invasion & Metastasis Research, Cancer Institute of Capital Medical University.
Professor Malcolm D Mason

Dean of Research in Life Sciences and Health, at Cardiff University
Cancer Research Wales Professor of Clinical Oncology
Professor of Institute of Cancer & Genetics of Cardiff University

Malcolm Mason is the Cancer Research Wales Professor of Clinical Oncology, and Dean of Research in Life Sciences and Health, at Cardiff University. He graduated from St Bartholomew’s Hospital in London, and trained in Oncology at the Institute of Cancer Research & Royal Marsden Hospital. He is the current chair of the UK National Cancer Research Network Prostate Cancer Clinical Studies Group. He has been responsible for a several practice-changing national and international clinical trials in cancer, most notably the recent intergroup study which demonstrated that radiotherapy could halve the mortality from locally advanced prostate cancer. He is the Director of the Wales Cancer Bank, the first national population-based tumour bank to be launched in the UK. He also works for the Union for International Cancer Control on their TNM programme for cancer staging, for which he is the Co-Chair of the Process Task Force, a member of the Core Group, and the Chairman of the UK National TNM Committee.

 Malcolm Mason, an old classmate of mine, is the head of the Department of Oncology at the Royal Marsden Hospital in London. He graduated from St. Bartholomew’s Hospital in London, and trained in Oncology at the Institute of Cancer Research & Royal Marsden Hospital. He is the current chair of the UK National Cancer Research Network Prostate Cancer Clinical Studies Group. He has been responsible for several practice-changing national and international clinical trials in cancer, most notably the recent intergroup study which demonstrated that radiotherapy could halve the mortality from locally advanced prostate cancer. He is the Director of the Wales Cancer Bank, the first national population-based tumour bank to be launched in the UK. He also works for the Union for International Cancer Control on their TNM programme for cancer staging, for which he is the Co-Chair of the Process Task Force, a member of the Core Group, and the Chairman of the UK National TNM Committee.
吴以岭 院士

中国工程院院士，河北省中西医结合医药研究院院长，中医药学学科创立者和学科带头人，两项国家973计划项目首席科学家，国家中医药管理局病研究重点实验室主任，兼任中国中西医结合学会副会长、中华中医药学会副会长，中华中医药学会络病分会主任委员、中国中西医结合血管脉络病专委会主任委员，世界中医药学会联合会络病专委会会长。

**Professional Distinctions**
Academician, Chinese Academy of Engineering
President, Hebei Academy of Integrative Chinese and Western Medicine
Founder, Discipline of Collateral Disease Theory in Practice
Chief scientist for two national natural science foundation projects (973)
Head, Key Laboratory of Collateral Diseases, State Administration of Traditional Chinese Medicine

**Professional Affiliations**
Vice chairman, Chinese Association of the Integration of Traditional and Western Medicine
Vice chairman, China Association of Chinese Medicine
Director, Collateral Disease Branch, China Association of Chinese Medicine
Director, Vessel-Collateral Specialty Committee, Chinese Association of the Integration of Traditional and Western Medicine
Director, Collateral Disease Specialty Committee, World Federation of Chinese Medicine Societies
Professor Wen G Jiang

Professor Jiang graduated from Peking University Health Science Centre (Previously Beijing Medical University) and received his MD degree from the University of Wales College of Medicine (Presently Cardiff University). Since 1989, he has been a research fellow, senior research fellow, senior lecturer and from 2004, Professor. He is the Director of the Cardiff University-Peking University Cancer Institute, Academic Director of International Relations of Cardiff University and is an honorary professor of Peking University, Capital Medical University and Inner Mongolia Medical University, and an international consultant for the Beijing Lung Cancer Centre. Professor Jiang is a Fellow of Royal Society of Medicine, Fellow of the Society of Biology and has received awards for Man of the Year in Medicine. He has created the China Medical Scholarship in the UK which is devoted to UK-China collaboration in medicine, medical research and education. These collaborations have won the TIMES Higher Education International Collaboration of the Year. He is a member of the British, American and European Societies of Cancer Research. Professor Jiang is the chief editor of Cancer Metastasis, Journal of Molecular and Genetic Medicine and sits on the editorial board of more than 20 international journals. His main interest is cancer metastasis and angiogenesis and, cancer genetic therapies. He has authored and co-authored 5 books and more than 500 SCI publications.

Professor Jiang is a celebrated medical researcher with significant contributions to the field. He has been involved with various research institutes and universities, contributing to the advancement of medical knowledge. His work has been recognized with numerous awards and has established his reputation as a leading expert in his field.
中英肿瘤研究交流大事记
Memorable Events of the Sino-UK Cancer Exchanges

联合生物医学中心
Joint Center for Biomedical Research

2012年5月，首都医科大学卡迪夫大学联合生物医学中心揭牌仪式
2012 May, Launch of CMU's Cardiff University-Capital Medical University Joint Centre for Biomedical Research.

2013年4月，王晓民校长一行赴卡迪夫大学参加卡迪夫大学—首都医科大学联合生物医学中心启动仪式
The launch event of Cardiff University-Capital Medical University Joint Centre for Biomedical Research in April 2013 in Cardiff.

2012年5月，卡迪夫大学David Grant博士、医学院院长Paul Morgan教授、姜文国教授和Sandra Elliott教授参观首都医科大学卡迪夫大学联合生物医学中心
2012 May, Cardiff's V-C Dr David Grant, Cardiff's Med Dean Professor Paul Morgan, Professor Jiang and Professor Sandra Elliott visited to Capital Medical University- Cardiff University Joint Centre.
2013 October, UHB/NHS colleagues visited the Cardiff University-CMU Joint Centre for Biomedical Research at CMU’s research building.
教育合作签约
Signing of an MOU of Cooperation in Education

2013年10月，首医医科大北京大学签署教育合作协议
2013 October, signing of an MOU of cooperation in Education between Cardiff University and CMU.
学术讲座和荣誉聘任

Academic Lectures and Honorary Appointment

2012年9月，卡迪夫大学主席、诺贝尔奖获得者Martin Evans爵士率团访问首都医科大学并进行学术讲座，并受聘担任首都医科大学荣誉教授。

2012 September, CMU Cardiff's President, Nobel winner Sir Martin Evans visited to Capital Medical University with his colleagues and gave a Noble Lecture on Stem cell. Sir Martin Evans was awarded Honorary Professorship.
2010年，卡迪夫校长David Grant受聘担任首都医科大学荣誉国际顾问
Dr David Grant, Cardiff’s Vice-Chancellors received international advisory role from Capital Medical University in 2010.

2011年，首都医科大学校长吕兆丰受聘担任卡迪夫大学荣誉院士
Award of Cardiff Honorary Fellowship to Professor Zhaofeng Lu, 2011.

2013年，首都医科大学校长王晓民受聘担任卡迪夫大学荣誉教授
Award of Cardiff Honorary Professorship to Professor Xisomin Wang, 2013.

2013年，卡迪夫校长Colin Riordan受聘担任首都医科大学荣誉国际顾问
Professor Colin Riordan, Cardiff’s V-C and President received the International Advisor in 2013.
卡迪夫中国医学奖学金
Cardiff's China Medical Scholarship

2010年，在人民大会堂广东厅举行卡迪夫中国医学奖学金结业证书颁发典礼
Cardiff’s China Medical Scholarship award event 2010, Guangdong Hall of the Great Hall of the People.

2012年，在人民大会堂北京厅举行卡迪夫中国医学奖学金结业证书颁发典礼
Cardiff’s China Medical Scholarship award event 2012, Beijing Hall of the Great Hall of the People.
2014年，中国医学学者赴卡迪夫大学访问交流
Medical scholars at Cardiff University, 2014.

获奖
Prize

2011年，卡迪夫中国医学奖学金及卡迪夫—中国在医学和肿瘤研究领域的国际合作，获得英国“泰晤士高等教育奖”中的“国际合作奖”
Cardiff’s China Medical Scholarship and international collaboration with China in medical and cancer research received the TIMES Higher Education International Collaboration of the Year in 2011.
学生及学者交流
Student and scholar exchanges

2009年，首都医科大学访问学者赴卡迪夫大学访问交流
CMU scholars at Cardiff University 2009.

2012年，首都医科大学研究生赴卡迪夫大学访问交流
CMU postgraduates at Cardiff University 2012.

2013年，卡迪夫大学博士生赴首都医科大学访问交流
Cardiff's PhD at Capital Medical University 2013.
2013年，卡迪夫大学学生在英国驻北京使馆庆祝NHS成立65年纪念会
Cardiff's students at the British Embassy in Beijing celebrating NHS 65th birthday.

2014年，中国大学访问学者赴卡迪夫大学访问交流
CMU scholars at Cardiff University, 2014.

卡迪夫中国校友会活动
Activities of Cardiff’s China Medical Alumni

2012年9月，卡迪夫中国校友会聚会
Cardiff's China Medical Alumni Association, September 2012.
Declined expression on hepatic stimulator substance (HSS) promotes metastasis of hepatocellular carcinoma through the activation of ERK molecule

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Department of Cell Biology and Municipal Laboratory for Liver Protection and Regeneration Regulation, Capital Medical University, 100069 Beijing, China

Background and Aims The poor prognosis of hepatocellular carcinoma (HCC) is mainly due to tumor recurrence and metastases. Recently, epithelial-mesenchymal transition (EMT) has been implicated in tumor invasion and metastasis. However, the underlying molecular mechanisms are yet to be elucidated. Hepatic stimulator substance (HSS) has been considered as an important intracellular survival factor for hepatocytes and promotes liver regeneration after liver damage or partial hepatectomy. However, it is not clear yet whether HSS plays a role in the development of HCC. The aim of this study is to investigate the relationship between HSS expression and HCC metastasis, clarify the mechanisms in this process, and provide theoretical basis for the HSS as a pharmaceutical drug target for the treatment of HCC.

Methods We first detected HSS expression in HCC samples in different clinical stages through real-time PCR. And then, we constructed two cell lines, the HSS-expressing cells which was established by stable transfection of HSS-containing plasmid and a HSS-knockdown cell by transfecting of a HSS-shRNA plasmid. We examined the morphology of cell and organelle structure through scanning electron microscopy (SEM) and transmission electron microscopy (TEM), and investigated relationship between HSS expression and HCC cell migration/invasion through transwell assay. Meanwhile, we successfully constructed orthotopic transplanted tumor model to determine the relationship between HSS expression and the tumor metastasis in vivo. Subsequently, we detected the gradual changes of several EMT markers and transcription factors to check the relationship between HSS expression and occurrence of EMT. Moreover, we also detected extracellular signal-regulated kinase (ERK) and serine/threonine-specific protein kinase (AKT) signaling pathways to see if they are involved in the EMT process which was provoked by a decrease in HSS expression.

Results Here, we show the expression of HSS obviously decreased in BCLC-C stage, the period tumor metastasis had occurred. Meanwhile, compared with HSS-expressing cells, the HSS-knockdown cells have much longer and more pseudopodia. Transwell assay also showed HSS decrease could promote HCC cells invasion and migration. Through orthotopic transplanted tumor assay, we demonstrated the low expression of HSS in HCC cells have stronger ability of metastasis and the mouse injection with the cells emaciated and died quickly. Moreover, the low expression of HSS resulted in the expression of epithelial cell markers decreased, mesenchymal cells markers up-regulated, and the phosphorylation of ERK was significantly increased. And the migration and invasion of the cells was significantly decreased after added ERK inhibitor, PD98059. Conclusion Taken together, our results suggest the decreased expression of HSS was able to induce the occurrence of EMT, which is highly related with the activation of ERK molecule.

Keywords] hepatic stimulator substance (HSS); hepatocellular carcinoma (HCC); metastasis; epithelial-mesenchymal transition (EMT); extracellular signal-regulated kinase (ERK)
Elevated expression of U1I/UTR in human hepatocellular carcinoma and its possible mechanisms

Xiaotong Yu, Pengyan Wang, Hongxia Wang, Ying Jiang, Xuejing Wang*

Cancer Institute, Capital Medical University, Beijing 100069, China

**Aim** Our previous study has shown that UII/UTR system was up-regulated in precancerous liver lesions and that UII could stimulate the proliferation of HOCs via a PKC-or ERK1/2-dependent pathway. In order to study the effect of UII/UTR on the proliferation of HOCs and the mechanism by which UII promoted liver cancer, we detected the expression of UII/UTR in human hepatocellular carcinoma, and further investigated the mechanisms involved in hepatocarcinogenesis. **Method** (1) HE staining: HE staining showed the normal structure of lobules destroyed and pseudolobules formed in liver tumor adjacent tissue sections, and also the size and shape of hepatic cells that were abnormal, the pathological karyokinesis and tumor giant cell in liver cancer tissue sections. (2) The expression of UII/UTR in cancer and tumor adjacent tissue: Immunohistochemical staining revealed that immunoreactive UII was localized to cytoplasm of liver, and the expression of UII protein was little in tumor adjacent tissue, while abundant in cancer tissue. UII and UTR mRNA were significantly elevated in cancer tissue compared with tumor adjacent tissue (p<0.05). Western blot analysis revealed that UTR expression enhanced in cancer tissue compared with tumor adjacent tissue(p<0.05). (3) PKC, ERK1/2, and p38MAPK expression: Western blot analysis revealed that the phosphorylation of PKC, ERK1/2 and p38MAPK in cancer tissue increased 2.4, 1.5, and 1.3-fold compared with control (p<0.05). (4) Serum-deprived oogonium cells were treated with 10-7 M UII for 24h, Western blot assay showed the expression of c-myc, c-jun and c-fos significantly increased. **Conclusion** Our studies showed the UII/UTR system was up-regulated in HCC, and UII may therefore be the pathogenesis factor of HCC as an autocrine/paracrine growth factor. UII increased PKC, ERK1/2, and p38MAPK protein phosphorylation involving in the proliferation of HOCs. UII also activated oncogene expressions in liver cells, such as c-myc, c-jun, and c-fos, leading to occurrence of liver cancer.
The Effect of oxidative stress on hepatic oval cells malignant transformation and the intervention of traditional Chinese medicine abstract

Xiaowei Xue, Pengyan Wang, Yuying Han, Xuejing Wang*

Cancer Institute, Capital Medical University, Beijing 100069, China

Aim We aimed to determine the whether reactive oxygen species involve in the malignant transformation of hepatic oval cells. To investigate the mechanism of this malignant transformation, we detected the hepatic oval cells heterotype changes, free radical injury, cell pathways involved in it, and the mechanisms of the mistletoe alkaloids and mistletoe polysaccharides in scavenging oxygen free radicals and regulating hepatic oval cell proliferation and differentiation.

Methods Cultured rat liver oval cell line WB-F344 (referred to as WB cells), were divided into complete medium group, free-serum medium group and hydrogen peroxide stimulation group. The normal WB cells could be transformed by stimulation of $7\times10^{-7}$ M $H_2O_2$ under cultured condition of free serum medium. The effect of $H_2O_2$ in promoting proliferation of WB cells was investigated by using MTT colorimetric analysis; WB cells were simulated continuously with $H_2O_2$ of low concentration, once a day, totally 21 times. The transformation effect was tested by morphologic observation, anchorage-independent growth assay, the changes of the cell cycle and the proportion of aneuploid cells by using flow cytometry and the expression of alpha-fetoprotein (AFP) by using Western blot. Trypan blue exclusion method was used to assess cell viability. Several tests were used to explore the effect of MP and MA on the malignant WB cells. The proliferation of malignant WB cells inhibited with MP and MA was observed by MTT assay. Intracellular ROS generation on different conditions was detected on flow cytometry using DCFH-DA as fluorescence probe; the concentration of hydroxyl radicals of the supernatant was tested by determination kit; alpha-fetoprotein (AFP), p-P53, P21, cyclin E, and DNA damage repair enzyme 8-oxo-G DNA glycosylase (8-oxoguanine DNA glycosylase, OGG1) were examined by using Western blot.

Results MTT results showed that proliferation of WB cells was induced obviously by $7\times10^{-7}$ M $H_2O_2$ for 12h and trypan blue staining showed that the viability of WB cells was up to 90%. Several transformation stands were used to test the malignant transformation effect. In morphology, the cells became anomalous and different in size, the ratio of nuclear to cytoplasm increased, and the cells growth polarities disappeared. In methylcellulose medium culture, the cells could form clone in the medium. In flow cytometry, G1 phase cells decreased, S phase cells increased and the proportion of aneuploid cells increased ($P<0.05$). At the same time, the intracellular ROS was increased. The results of western blot showed that AFP expression was increased ($P<0.05$) and OGG1 was decreased. Both MP and MA inhibited the proliferation of the malignant WB cells in a time and dose-dependence manner with MTT assay, while with trypan blue exclusion test as quality control, we found that after the treatment of MP 5 g/L and MA 12 g/L for 72 h, cell survival rate was 80%. The results of flow cytometry showed that MA and MP reduced the number of S-phase cells, increased G1 phase cells and decreased intracellular ROS ($P<0.05$). The inhibited ability of hydroxyl radicals was increased in cell supernatants ($P<0.05$), MA and MP could enhance the expression levels of p-P53 and P21, inhibited the tumor marker AFP and cyclin E ($P<0.05$). But the expression of OGG1 did not change significantly between malignant cell group and drug intervention group. Conclusion Microenvironment impacts the differentiation and proliferation of hepatic oval cells. Minidose hydrogen peroxide stimulated the WB cells for some times, the level of intracellular ROS could increase, then causing cell cycle-related proteins and DNA repair damage enzymes express abnormally, finally, leading to the hepatic oval cells malignant transformation. It was indicated that ROS, which regulated the hepatic oval cell proliferation and differentiation, could make an important part in the hepatic oval cells malignant transformation. MP and MA can inhibit the proliferation of the malignant cells, and induce these cells differentiating from the immature to mature in the same times. Its possible mechanism was that MA and MP can scavenge the oxygen free radicals of the cell microenvironment, reduce ROS level of the intracellular, and regulate cell cycle, and ultimately affect the hepatic oval cells proliferation and differentiation.
Analysis of the relationship between microsatellite instability and thymic lymphoma induced by N-methyl-N-nitrosourea in C57BL/6J mice

Xueyun Huo, Shuangyue Zhang, Zhenkun Li, Juan Gao, Chao Wang, Changlong Li, Meng Guo, Xiaoyan Du*, Zhenwen Chen*

Department of Laboratory Animal Science, School of Basic Medical Sciences, Capital Medical University, Beijing, China.

Microsatellite instability (MSI) has been found to be closely associated with many types of human tumors and often shows strong correlations with specific tumor features. However, whether MSI is caused by tumors or tumor-causing factors and whether a relationship exists between MSI and tumors are still unclear. The aim of the present study was to explore the relationships between MSI, tumor formation and the mutagenic effects of N-methyl-N-nitrosourea (MNU). Mice were administered either MNU (90 mg/kg) or PBS and DMSO (control) at the beginning of the 1st week of the experiment. Of the 31 mice that survived the entire experimental time course, 19 (61.3%) mice developed thymic lymphomas. In addition, 52.6% (10/19) of the tumors had metastasized to the liver. We detected MSI in MNU-treated mice using a panel of 42 mutation-sensitive loci. Nineteen loci (45.2%) in six organs showed 70 MSI events. Locus D8Mit14 showed enhanced MSI compared with the other examined loci. MSI frequency in the thymus was higher than in other organs. Interestingly, the MSI frequency (23/12/42, 4.6%) in normal thymus tissue was significantly higher than in thymic lymphoma tissue (4/19/42, 0.5%) (p<0.0001). There was no difference between non-metastasis livers and metastatic livers. These results in thymus illustrate that in MNU-treated mice, MSI was enhanced in non-tumor samples compared with tumor samples. These findings indicates that MSI is not only associated with tumor group but also occurs more commonly in non-tumor group under the same chemically induced conditions.

[Keywords] N-methyl-N-nitrosourea (MNU); microsatellite instability (MSI); thymic lymphoma; metastasis; C57BL/6J mice
Thymic lymphoma model induced by N-methyl-N-nitrosourea in C57BL/6J mice

Xueyuan Huo, Shuangyue Zhang, Zhenkun Li, Juan Gao, Jing Lu, Chao Wang, Changlong Li,
Meng Guo, Xiaoyan Du, Zhenwen Chen

Department of Laboratory Animal Science, School of Basic Medical Sciences, Capital Medical University, Beijing, China

N-methyl-N-nitrosourea (MNU) induced tumor is one of widely used animal models for researching cancers, especially thymic lymphoma. However, the disadvantage of current protocol is that it takes too long to get higher tumor incidence and the administrations were in disorder. The aim of the present study was to reduce the model reproducing time and optimize the administration protocol in C57BL/6J mice. Mice were randomly divided into single high-dose group (SH, administered MNU 90 mg/kg at 1st week) and continuous low-dose group (CL, administered 60, 40, 20 mg/kg MNU at 1st, 4th, and 7th week, respectively), and their solvent controls (SHC and CLC). By the end of the 16th week, mice in MNU-treated groups exhibited significant low body weight (pSH<0.001; pCL<0.01) and poor lifespan compared with controls. Thymic lymphomas was successfully developed in both groups of MNU-treated mice (SH, 64.3%; CL, 75.0%) (pSH<0.001; pCL<0.001). In addition, totally 91.9% thymic lymphoma spread to important organs. Among which, the ratio of the tumor spreading to spleen (86.5%) is significantly higher than to liver (40.5%) (p<0.001) and kidney (29.7%) (p<0.001), indicating that spleen was the major target of thymic lymphoma metastasis in MNU-treated mice. Neither lifespan, nor the tumorigenesis and metastasis rate of thymic lymphomas to the major organs between SH and CL was insignificant difference (P>0.05). In conclusion, we developed a set of protocols in C57BL/6J mice to produce thymic lymphomas model in shorten time.

Keywords] C57BL/6J mice; N-methyl-N-nitrosourea; thymic lymphoma
Human chorionic gonadotropin β (hCGβ) promotes tumorigenesis in a variety of tumors including glioblastoma, breast and prostate cancer cells, etc. However, the involved mechanisms remain elusive. Different from the other tumors, glioblastoma is a highly invasive brain tumor; invasion causes high recurrence and mortality. Characterization of hCGβ signalling is to determine therapeutic targets to inhibit invasion and lower recurrence. Through both a stable cell line over-expressing hCGβ and hCGβ standards, we tested hCGβ signalling, migration, and invasion in human glioblastoma U87MG cells. ELISA showed that hCGβ secreted into culture medium at an amount of 237.8±7.8 ng/10^7 cells in hCGβ transfected stable cells after the cells were grown for 24 h. Through Western blot and Gelatin zymography, we found that HCGβ standards phosphorylated ERK1/2 and upregulated MMP-2 expression in dose- and time-dependent manner. Meanwhile, overexpressed hCGβ phosphorylated ERK1/2, and upregulated MMP-2 expression and activity, whereas ERK1/2 blocker PD98059 (25 μM) significantly decreased both ERK1/2 and MMP-2 expression and activity. In addition, in the same conditions as the signalling test, hCGβ promoted cell migration and invasion, whereas the PD98059 diminished these effects. These findings demonstrated that hCGβ phosphorylated ERK1/2 upregulating MMP-2 expression and activity leading to cell migration and invasion, suggesting that hCGβ, ERK1/2 and MMP-2 are the potential targets to inhibit glioblastoma invasion.

**Keywords** human chorionic gonadotropin β; invasion; ERK1/2; MMP-2; glioblastoma
**Sulforaphane inhibits invasion via activating ERK1/2 signaling in human glioblastoma U87MG and U373MG cells**

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**Background** Glioblastoma has highly invasive potential, which might result in poor prognosis and therapeutic failure. Hence, the key we study is to find effective therapies to repress migration and invasion. Sulforaphane (SFN) was demonstrated to inhibit cell growth in a variety of tumors. Here, we will further investigate whether SFN inhibits migration and invasion and find the possible mechanisms in human glioblastoma U87MG and U373MG cells. **Methods** First, the optimal time and dose of SFN for migration and invasion study were determined via cell viability and cell morphological assay. Further, scratch assay and transwell invasion assay were employed to investigate the effect of SFN on migration and invasion. Meanwhile, Western blots were used to detect the molecular linkage among invasion related proteins phosphorylated ERK1/2, matrix metalloproteinase-2 (MMP-2) and CD44v6. Furthermore, Gelatin zymography was performed to detect the inhibition of MMP-2 activation. In addition, ERK1/2 blocker PD98059 (25 \(\mu\)M) was integrated to find the link between activated ERK1/2 and invasion, MMP-2 and CD44v6. **Results** The results showed that SFN (20 \(\mu\)M) remarkably reduced the formation of cell pseudopodia, indicating that SFN might inhibit cell motility. As expected, scratch assay and transwell invasion assay showed that SFN inhibited glioblastoma cell migration and invasion. Western blot and Gelatin zymography showed that SFN phosphorylated ERK1/2 in a sustained way, which contributed to the downregulated MMP-2 expression and activity, and the upregulated CD44v6 expression. These molecular interactions resulted in the inhibition of cell invasion. Conclusions SFN inhibited migration and invasion processes. Furthermore, SFN inhibited invasion via activating ERK1/2 in a sustained way. The accumulated ERK1/2 activation downregulated MMP-2 expression and decreased its activity and upregulated CD44v6. SFN might be a potential therapeutic agent by activating ERK1/2 signaling against human glioblastoma.

**Keywords** glioblastoma; ERK1/2 phosphorylation; matrix metalloproteinase-2 (MMP-2); CD44v6; invasion.
Uncoupling protein 2 may contribute to hepatoma cells autophagy

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It is well known that mitochondrial uncoupling protein 2 (UCP2) interfere with mitochondrial synthesis of adenosine triphosphate and suppress the generation of superoxide. UCP2 becomes highly abundant in some cancers, and may further modulate energy metabolism in response to high reactive oxygen species levels in cancer cells and promote chemoresistance. Autophagy is an important mediator of pathological responses and is engaged in cross-talk with reactive oxygen species in cell signaling and protein damage. This study aims to investigate the relationship between UCP2 and hepatoma cells autophagy in palmitic acid (PA)-induced lipotoxicity. Results demonstrated that UCP2 was associated with autophagy during PA-induced in hepatoma cells injury. Tests on reactive oxygen species (ROS) showed that UCP2 expression strongly decreases ROS production, and that PA-induced autophagy participates in this progress. Meanwhile, cell apoptosis increased, indicating that UCP2 may be involved in hepatoma cells lipotoxicity. Furthermore, in PA-induced cell damage, over-expression of UCP2 decreased cell apoptosis. In conclusion, increasing UCP2 expression in hepatoma cells may contribute to cell autophagy and anti-apoptotic as result of fatty acid injury. UCP2 may contribute to the selection of cancer cells with enhanced adaptive abilities. Our results may bring new insights for hepatic carcinoma therapies.
Suppressed microRNA-320a in GBM patients modulates glioma cell functions by targeting IGF-1R

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Glioblastoma (GBM) is the most aggressive and malignant glioma. Currently, a few modern surgical and medical therapeutic strategies are applied for GBM, but the prognosis of GBM patients remains poor, and the average median survival time is only 14.6 months. In this study, we for the first time found that the levels of MiR-320a were decreased in both GBM patients and glioma cells. In GBM patients, elevated MiR-320a expression was associated with better prognosis. In addition, IGF-1R was identified as a key direct target of MiR-320a. Overexpression of MiR-320a led to the inhibition of cell proliferation, migration, invasion, as well as tumorigenesis by targeting IGF-1R, and thus regulated the signaling pathways downstream, including PI3K/AKT and MAPK/ERK. In tumor orthotopic xenograft experiment, the tumor growth was depressed and survival time of mice model was prolonged when MiR-320a was over-expressed. Therefore, our results suggested that MiR-320a could suppress tumor development and growth by targeting IGF-1R and MiR-320a might serve as a new effective target for anticancer therapy strategies.
Decreased expression of MicroRNA-206 regulates cell proliferation via cyclin D2 in gliomas

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MicroRNAs are short single-strand non-coding RNAs which regulate gene expression. De-regulation of microRNAs has been associated widely with many kinds of tumor generation. Glioblastoma (GBM) is a kind of highly lethal brain tumor with overall survival time about 12-14 months. To investigate abnormalities of MicroRNAs in this malignant disease, we performed MicoRNA specific microarray on 198 glioma patient’s samples. We identified that MicroRNA-206 (MiR-206) is down-regulated in high grade GBM (HGGs, including grade III and IV) by comparing to low grade glioma (grade II). Depressed expression of MiR-206 is associated with worse prognosis of GBM patients. Our results also showed transfection of MiR-206 into GBM cells causing down-regulation of cyclinD2 expression. Depressed CyclinD2 expression is also correlated well with lower MiR-206 level in GBM tumor samples. Transfection of MiR-206 in to GBM cell line leads to G1 arrest. In conclusion, this study shows MiR-206 expression is generally depressed in high grade GBM patients, this abnormality is significantly correlated with worse prognosis of GBM patients; one possible mechanism of this effect is losing regulation of cyclinD2 expression by MiR-260 leading to loss of cell cycle control.
MAGI3 negatively regulates Wnt/β-catenin signaling and suppresses malignant phenotypes of glioma cells

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Gliomas are the most common primary brain malignancies with a poor prognosis, in which aberrant activation of Wnt/β-catenin signaling is usually involved, but little is known about the regulation mechanisms Wnt/β-catenin signaling in gliomagenesis. In this study, we showed the downregulation of PDZ protein MAGI3 expression both at the mRNA and protein levels in human glioma samples, and found that MAGI3 could inhibit proliferation, migration, and cell cycle progression of glioma cells in both MAGI3 overexpression and siRNA knockdown studies. Also, MAGI3 overexpression inhibited the growth of C6 glioma tumour xenograft in nude mice. Moreover, we demonstrated a physical interaction between MAGI3 and β-catenin mediated by the PDZ domains of MAGI3 and the PDZ-binding motif of β-catenin by using GST pull-down and Co-IP assays. By interaction with β-catenin, MAGI3 could suppress β-catenin-TCF-mediated transcription and subsequent the expression of β-catenin target genes, such as cyclin D1 and axin2 in glioma cells, and C6 glioma tumour xenograft in nude mice. Furthermore, Survival analysis based on the GEO glioma dataset revealed that patients with high (above median) MAGI3 expression had longer overall survival than those with low MAGI3 expression. Tumor grade and MAGI3 mRNA level were negatively correlated. Overall, these results identify MAGI3 as a novel tumor suppressor in glioma and provide more insights into the pathogenesis of glioma.
NHERF1 regulates actin cytoskeleton organization by modulating stability of α-actinin 4

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The adaptor protein NHERF1 (Na⁺/H⁺ exchanger regulatory factor 1) was recently found as an important player in the actin cytoskeleton networks. To clarify the role of NHERF1 on actin cytoskeleton organization and identify the differently expressed proteins of cytoskeleton assembly regulated by NHERF1, NHERF1 RNAi knockdown and overexpression assays, 2-DE combined with MALDI-TOF-MS assays, GST pull-down, co-immunoprecipitation and immunofluorescence assays were performed in this study. Results found that NHERF1 regulated F-actin fiber organization via direct interaction with actin cross-linking protein α-actinin 4. This interaction promoted the ubiquitination of α-actinin 4 and resulted in disassemble the organization of actin fibers. Our findings discover a new NHERF1-associating protein-α-actinin 4, and reveal a novel mechanism of α-actinin 4 regulation by which its expression is modulated at the post-translational level by ubiquitination, and clarify the role of NHERF1, which directly binds to α-actinin 4, promoting the ubiquitination and subsequent degradation of α-actinin 4, further resulting in disassembly of F-actin and disruption of actin cytoskeleton.
Role of C-KIT receptor in the development of colorectal cancer

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C-KIT receptor, which belongs to type III receptor tyrosine kinase, plays an important role in the development of multiple tumors. However, its role in colorectal cancer (CRC) remains controversial: some researchers considered C-KIT receptor may contribute to the proliferation and invasion of CRC, while others hold an opposite view. To address this question, we investigated the C-KIT receptor and its downstream signaling pathways by the use of CRC mouse model (Wads/-) deficient in C-KIT receptor induced by AOM+DSS and human CRC cell line, HCT116. We found that the tumors collected from Wads/- mice showed less mucilage cavities and lower degree of malignant than those from wide type (WT) mice. We also observed decreased ETV4 expression in Wads/- mice, accompanied by much milder tumor growth and invasion. Likewise, after treatment with Imatinib, the inhibitor of C-KIT, the proliferation, migration and invasion of HCT116 cells were significantly suppressed, probably due to stabilizing ETV4 through MEK/ERK signaling pathway. In conclusion, our findings reveal a key role of C-KIT receptor/ETV4 signaling in the development of CRC.

[Keywords] C-KIT receptor; CRC; ETV4; Wads
The tyrosine kinase c-Src directly mediates growth factor-induced Notch-1 and Furin interaction and Notch-1 activation in pancreatic cancer cells

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The proteolytic activity of Furin responsible for processing full length Notch-1 (p300) plays a critical role in Notch signaling. The amplitude and duration of Notch activity can be regulated at various points in the pathway, but there has been no report regarding regulation of the Notch-1-Furin interaction, despite its importance. In the present study, we found that the Notch-1-Furin interaction is regulated by the non-receptor tyrosine kinase, c-Src. c-Src and Notch-1 are physically associated, and this association is responsible for Notch-1 processing and activation. We also found that growth factor TGF-α, an EGFR ligand, and PDGF-BB, a PDGFR ligand, induce the Notch-1-Furin interaction mediated by c-Src. Our results support three new and provocative conclusions: (1) The association between Notch-1 and Furin is a well-regulated process; (2) Extracellular growth factor signals regulate this interaction, which is mediated by c-Src; (3) There is cross-talk between the plasma growth factor receptor-c-Src and Notch pathways. Co-localization of Notch-1 and c-Src was confirmed in xenograft tumor tissues and in the tissues of pancreatic cancer patients. Our findings have implications for the mechanism by which the Notch and growth factor receptor-c-Src signaling pathways regulate carcinogenesis and cancer cell growth.

Keywords] Notch; c-Src; pancreatic cancer
Correlation between DNase I hypersensitive site distribution and gene expression in HeLa S3 cells

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Mapping DNase I hypersensitive sites (DHSs) within nuclear chromatin is a traditional and powerful method of identifying genetic regulatory elements. DHSs have been mapped by capturing the ends of long DNase I-cut fragments (>100,000 bp), or 100-1200 bp DNase I-double cleavage fragments (also called double-hit fragments). But next generation sequencing requires a DNA library containing DNA fragments of 100-500 bp. Therefore, we used short DNA fragments released by DNase I digestion to generate DNA libraries for next generation sequencing. The short segments are 100-300 bp and can be directly cloned and used for high-throughput sequencing. We identified 83,897 DHSs in 2,343,479 tags across the human genome. Our results indicate that the DHSs identified by this DHS assay are consistent with those identified by longer fragments in previous studies. We also found: (1) the distribution of DHSs in promoter and other gene regions of similarly expressed genes differs among different chromosomes; (2) silenced genes had a more open chromatin structure than previously thought; (3) DHSs in 3' untranslated regions (3'UTRs) are negatively correlated with level of gene expression.

Keywords] DNase I hypersensitive site; gene expression; regulation
Lamin A/C protein is overexpressed in tissue-invading prostate cancer and promotes prostate cancer cell growth, migration and invasion through the PI3K/AKT/PTEN pathway

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Prostate cancer (PC) remains the second most common cause of cancer-related death in Western countries. A previous proteomics study suggested that the nuclear membrane protein lamin A/C to be a maker to discriminate low- and high-Gleason score tumors and to identify high-risk cancers. To characterize its function in PC cells, we performed a detailed expression analysis in PC tissue and explored the consequences of down or upregulation of lamin A/C in PC cells. Our results confirm an increased lamin A/C protein expression in high-risk cancers and show association of expression with tumor cell formations at the invasion fronts of tumors and in invasion "spearheading" tumor cell clusters. In the prostate tumor cell lines, LNCaP, DU145, and PC3 small hairpin RNA knockdown or overexpression of lamin A/C resulted in inhibition or stimulation, respectively, of cell growth, colony formation, migration and invasion. Further mechanism studies suggested that the lamin A/C-related malignant behavior is regulated through modulation of the phosphoinositide 3-kinase (PI3K)/AKT/PTEN signaling pathway. Western blot results indicated that knockdown or overexpression of lamin A/C decreased or increased, respectively, protein levels of the PI3K subunits p110 and p85 in all three cell lines; phosphor-AKT in the PTEN-negative cell lines LNCaP and PC3, and, increased or decreased, respectively, PTEN protein levels in PTEN-positive DU145 cells. Together, our data suggest that lamin A/C proteins are positively involved in malignant behavior of PC cells through the PI3K/AKT/PTEN pathway. Lamin A/C may represent a new oncogenic factor and a novel therapeutic target for PC.

Keywords: prostate cancer; laminA/C; PI3K
KITLG is a novel target of miR-34c that is associated with the inhibition of growth and invasion in colorectal cancer cells

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MiR-34c is considered a potent tumor suppressor due to its negative regulation of multiple target mRNAs that are critically associated with tumorigenesis and metastasis. In the present study, we demonstrated a novel target of miR-34c, KITLG, which has been implicated in colorectal cancer (CRC). First, we found a significant negative relationship between miR-34c and KITLG mRNA expression levels in CRC cell lines, including HT-29, HCT-116, SW480, and SW620 CRC cell lines. In silico analysis predicted putative binding sites for miR-34c in the 3' untranslated region (3'UTR) of KITLG mRNA. A dual-luciferase reporter assay further confirmed that KITLG is a direct target of miR-34c. Then, the cell lines were infected with lentiviruses expressing miR-34c or miR-34c specific inhibitor. Restoration of miR-34c dramatically reduced the expression of KITLG mRNA and protein, while silencing of endogenous miR-34c increased the expression of KITLG protein. The miR-34c-mediated down-regulation of KITLG was associated with the suppression on proliferation, cellular transformation, migration and invasion of CRC cells, as well as the promotion on apoptosis. Knockdown of KITLG by its specific siRNA confirmed a critical role of KITLG down-regulation for the tumor suppressive effects of miR-34c in CRC cells. In conclusion, our results demonstrated that miR-34c might interfere with KITLG-related CRC and could be a novel molecular target for CRC patients.

[Keywords] colorectal cancer cell; KITLG; miR-34c; tumor suppressor
Keap1 suppresses invasion and metastasis of NSCLC by stabilizing cytoskeleton and focal adhesions

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The expression of tumor suppressor Kelch-like ECH-associated protein1 (Keap1) is lower in non-small cell lung cancer (NSCLC). The role of Keap1 involved in invasion and metastasis of NSCLC remains unclear. In the present study, over-expression of Keap1 in A549 cells could stabilize the F-actin cytoskeleton and regulate focal adhesion distribution by mediating RhoA activity, thereby restrain the motility and invasion in A549 cells. Tumor xenograft models were established to further explore the role of Keap1 in the development and metastasis of tumor in vivo. We found that the tumor xenograft had smaller size and less metastasis in Keap1 over-expression mice. The above in vivo and in vitro studies both demonstrated that Keap1 can suppress tumor development and metastasis, which could provide new explanation for the mechanism of tumor metastasis in NSCLC.

[Keywords] Keap1; NSCLC; RhoA; cytoskeleton; focal adhesion
Preparation and characterization of novel adeno-associated viral vectors targeting to decorin-expressing cells

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Decorin (DCN) is a core protein shared by a great variety of small molecular weight family members of proteoglycans. DCN is leucine-rich in the amino acid composition, and is abundantly expressed in the extracellular matrix in numerous forms of polysaccharides. DCN serves as ligands of many types of cytokines and exerts important biological functions to influence cell growth, especially in cancers where high levels of DCN expression have been observed. Adeno-associated virus (AAV) is a common vector being applied in cancer therapies. Targeted infection of DCN-expressing tissues with AAV could be an attractive approach to selectively deliver therapeutic genes for cancer gene therapy. We have identified a DCN-binding motif (DB1) based on the consensus region among DCN-binding proteins (DBPs). By fusion of DB1 to the N-terminus of the VP2 capsid protein, we have successfully obtained the DB1-displaying recombinant AAV2 through a chimera pseudo-packaging strategy. The obtained viral vector with DB1 motif in the capsid was able to infect DCN-overexpressing cells with much increased efficiency. Our novel DCN-targeting AAV not only can be a useful vector for the consideration in cancer gene therapy applications, but can also be a helpful gene delivery tool in studies to investigate the functions of DCN during cancer development.

[Keywords] adeno-associated virus; decorin; gene therapy; motif; protein interaction
NAMPT inhibitor FK866 as a potent molecule to promote drug sensitivity to temozolomide in glioma cells

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Glioma is a primary brain tumor with most prevalence and poor prognosis. Temozolomide (TMZ) is the first-line chemotherapy drug to treat glioma patients post surgery. However, the failure of chemotherapy is often seen due to the development of tumor cell resistance to the cytotoxic effects of TMZ. Clinical studies indicated that elevated expression of the repair protein O6-methylguanine-DNA methyltransferase (MGMT) associated with TMZ resistance. Recently, FK866 was reported to play important roles in tumorigenesis, metastasis and chemoresistance in several cancer types, as a potent inhibitor of NAMPT (Nicotinamide phosphoribosyl transferase, the rate-limiting enzyme of salvage synthesis of NAD). In the present study, we found that patients with low NAMPT expression manifested a good prognosis independent of the levels of MGMT expression, based on the expression microarray data of 220 glioma samples of all grades from the Chinese Glioma Genome Atlas (CGGA). We further investigated whether FK866 was able to affect TMZ sensitivity in U87 human glioma cells. The results showed that a low single dose of 20 nM FK866 significantly increased TMZ-induced cell death. The IC50 of TMZ was decreased from 350 µM to 200 µM with the cotreatment of FK866. Meanwhile, increased level of cleaved PARP was observed. As FK866 is being trialed for lung cancer treatment, our findings suggested its potential application as a facilitating agent for glioma chemotherapy, especially for TMZ resistant cases.

【Keywords】FK866; NAMPT, glioma; TMZ; chemotherapy
Classic and non-canonical vascular endothelial growth factor signalling in related topathological angiogenesis

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The collective evidence suggests that the vascular endothelial growth factor (VEGF) family is critical for both increased vascular permeability and pathological angiogenesis. The VEGF family includes VEGF-A, -B, -C, -D, -E and placental growth factor (PIGF) which exist in a number of different isoforms with varying potency and specificity depending on local environmental cues and the particular vascular cell type involved. VEGFR-1 and VEGFR-2, the predominant VEGFRs in endothelial cells, have greater than 40% sequence homology VEGF receptors; VEGFR-1 (Flt-1), VEGFR-2 (KDR, Flk1), and VEGFR-3, show different specificity for VEGF family members. VEGF-A (hereafter referred to as VEGF) binds to VEGFR1 with higher affinity than VEGFR2. The classic view is that VEGFR2 regulates endothelial function and survival via a number of different canonical signalling pathways including Ras/ mitogen activated protein kinase (MAPK), Src, PI3K and NOS10 although this can be further modified through receptor heterodimerization and association with co-receptors neuropilin-1 and -2. VEGFR1 signalling is more complex because it 1) has only very weak kinase activity when compared to VEGFR-2, 2) is both a positive and negative regulator of angiogenesis dependent on the particular ligand binding (PIGF-1 inhibits angiogenesis while VEGF and PIGF-2 are proangiogenic), 3) can heterodimerize with VEGFR-2 and 4) participates in the anti-angiogenic activity of pigment epithelium-derived factor (PEDF).

Investigation of VEGF signalling has largely focused on the receptor binding events at or near the plasma membrane and subsequent activation of classical signal transduction cascades. However, we have made two exciting and novel observations. First, in endothelial cells, a dynamic translocation of VEGFRs to adheren junctions (AJs) and the nucleus occurs which is dependent on the balance of growth factors in the local microenvironments. Second, the ratio of VEGFR-1:VEGFR-2 is a major determinant of vascular permeability and angiogenesis. Subcellular translocation of VEGF receptors to adheren/tight junctions (AJs/TJs) results in VEGF receptors regulating vascular permeability. Moreover, nuclear translocation of VEGF receptors may regulate transcription of pro- and anti-angiogenic regulator. This is in agreement with a growing body of evidence that trafficking of receptor tyrosine kinase (RTKs) makes a critical contribution to their cellular function and provides an alternative non-canonical VEGF signalling. We hypothesized that VEGF-driven vascular permeability and angiogenesis are highly dependent on the ratio of VEGFR-1:VEGFR-2 within subcellular compartments. Endosomal sorting, γ-secretase and sumoylation appear to be key regulators of VEGFR trafficking. Pharmacological or genetic manipulation of components of the endosomal trafficking pathways will reduce vascular permeability and inhibit aberrant angiogenesis.
Anti-oestrogen resistance associated with deregulated CD44 and c-met expression in breast cancer

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Growth of the majority of breast tumours that express the oestrogen receptor (ER+) can be successfully inhibited with anti-oestrogen therapy. However, over time these tumours can relapse, acquiring endocrine resistance, often becoming independent of oestrogen signalling (ER-) with aggressive growth and metastasis which is difficult to treat. There is an urgent need to understand the biology associated with these changes with the aim of finding a therapeutic target for a group of ER- endocrine resistant patients where there is currently an unmet clinical need.

An in vitro endocrine-resistant model (FasR) was developed from the ER+ breast cancer cell line MCF7 by prolonged exposure to the anti-oestrogen drug fulvestrant. FasR cells lost ER expression (ER-) and displayed significantly increased migratory and invasive capability compared to the parental endocrine-responsive MCF7 cells. This was associated with increased tyrosine kinase receptor c-met signalling via hepatocyte growth /scatter factor (HGF/SF) which drives enhanced AKT signalling and aggressive behaviour. PCR and immunocytochemistry also demonstrated increased expression of the transmembrane receptor CD44 and its variant CD44v3 in FasR cells. Immunoprecipitation and immunofluorescent microscopy indicated an interaction between c-met and CD44 proteins. Furthermore, CD44 was a key modifier of the pro-invasive function of c-met in FasR cells since CD44 siRNA knockdown decreased basal and HGF induced met/AKT signalling and invasive capacity.

Gene expression analysis in a panel of breast cancer cell lines and PCR for CD44s/V3 in clinical breast cancer samples further demonstrated a direct association between c-met and CD44 with co-expression enriched in ER- breast cancer. Immunohistochemistry (IHC) focussing on CD44v3 protein demonstrated associations with reduced survival, poorer quality of response and shortened time to progression (TTP) from 49 to 23 months.

These data suggest CD44 deregulation is prominent in acquired endocrine resistant phenotypes, interplaying with c-met in ER- tumours to promote adverse behaviour. Further understanding and manipulation of the interaction between CD44 and its variants with c-met may be valuable in inhibiting cancer metastasis associated specifically with endocrine resistance.
Most cancer patients will be incurable after metastases occur. It is more likely that breast, prostate, lung, thyroid, and kidney cancers will spread to the bones. More than 2/3 of breast and prostate metastatic cancers will have bone metastasis. While approximately 1/3 of lung, thyroid, and kidney cancers will metastasize to the bone at the metastatic stage. The symptoms of bone metastases include severe pain, bone fractures, spinal cord compression, hypercalcemia, anemia, spinal instability, decreased mobility, and rapid degradation in the quality of life for patients. The mechanisms of bone metastasis remain mysterious despite intensive experimental studies. The majority of studies focus on osteoclast-mediated bone resorption and direct bone destruction. However, over 90% of our bone cells are osteocytes. Osteocytes are derived from osteoblasts which become trapped in the matrix they secrete. Osteocytes form an extensive cellular network throughout the bone matrix, from where they play a key role in determining osteoclast activity. Osteocytes produce factors, such as receptor activator of nuclear factor kappa-B ligand (RANKL), that signal to the osteoclasts to remove bone. Cytokines such as interleukin 1β increase RANKL in osteocytes in vitro. Osteocytes also affect osteoblasts. Mechanical loading decreases the production of catabolic factors, while it enhances nitric oxide (NO) production and Cox2 expression in osteocytes. It appears that apoptotic osteocytes recruit osteoclasts to initiate targeted bone resorption, which might be a critical signal to trigger bone remodelling. It is suggested that osteocyte apoptosis mediates osteoclast precursor adhesion to vascular endothelium by regulating osteocytic secretion of IL-6 and soluble IL-6 receptor (sIL-6R) to promote endothelial ICAM-1 expression. It is known that intensive cancer chemotherapy leads to significant bone loss. There is evidence that chemotherapeutic anti-cancer reagent methotrexate (MTX) induces apoptosis of osteocytes and increase osteoclast formation. Osteocytes appear to be enriched in hypoxia-resistant proteins and osteocyte hypoxia may play a role in disuse-mediated bone resorption. However, it is not known whether aggressive tumour cells divert or manipulate the crucial function of osteocytes in the maintenance of bone homeostasis.

We are interested whether aggressive tumour cells divert the transformation of osteoblasts to osteocytes, induce apoptosis of osteocytes under hypoxic microenvironment, or disturb the physical mediating role of osteocytes in the balance of osteoblasts and osteoclasts (through IL6 and RANKL signalling pathways?). We will further assess the hypothesis that osteocytes cannot act as a functional sensor of mechanical stress which leads to direct bone destruction. And we will also investigate whether osteocytes may secrete soluble factors which may stimulate the invasion and angiogenesis potentials of aggressive tumour cells in a feedback loop. We have observed that conditioned medium from osteocytes (MLO-Y4) following monolayer and 3D culture stimulated proliferation of some cancer cells. And osteocyte conditioned medium appeared to have an effect on tumour cell adhesion and invasion revealed by the ECI5 system. We are going to develop 3D culture models to better understand the interaction of tumour cells and osteoblast progenitor cells which can be directed to osteocytes. The phenotype of osteoblast-derived osteocyte-like cells will be assessed by expression profiling analysis of their early markers (e.g. DMP1 and GP38/E11) and late markers such as sclerostin (Sost) and Fibroblast growth factor 23 (FGF23). We will unveil the potential roles of osteocytes in tumour cell invasion and metastasis using a variety of cellular and molecular approaches.
MicroRNA changes during prostate cancer development in the PTEN knock out mouse.

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Prostate cancer (PCa) is the most common male cancer in the developed world – and is a leading cause of cancer-related deaths. Often, by the time the PCa becomes symptomatic, highly invasive surgery may be the only avenue available or hormonal therapy. PCa may be successfully treated with surgical resection but when the disease invades locally and spreads to the bone, the prognosis becomes very poor - eventually becoming refractory to these therapies. However, these are “late-stage” therapies for prostate cancer patients, and ideally we would like to identify changes in the disease much earlier in its development. Therefore, there is a clear need for early intervention in this disease.

MicroRNAs (miRs) are small RNAs that associate with the 3’ untranslated regions of their target mRNA and cause their degradation or translational inhibition. MiRs may regulate several miRNAs and each mRNA may be regulated by several miRs leading to a highly complex system. MiRs regulate a diverse set of biological events, from cell division, morphology to tissue development and differentiation, by influencing their target mRNA, and are often dysregulated in cancer cells.

We have used a mouse model for PCa (Probasin-Cre driven PTen deletion), which mirrors early human disease (30-60% approx.). Mice carrying prostate specific PTEN deletions develop high grade prostate intraepithelial neoplasia (PIN), leading to invasive tumours. Using a low-density array we screened all 700 mouse miRs in these prostate samples for changes in expression. We found several miRs to be highly overexpressed and several to be completely lost in tumour cells. Inhibitors of these overexpressed miRs were found to be able to reduce prostate cancer cell growth and cell motility in vitro, and to reduce xenograft growth in vivo.
MAGI proteins (Membrane Associated Guanylate Kinases) and their role in the invasiveness and metastasis of human colorectal cancer.

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MAGI (Membrane Associated Guanylate with Inverted Orientation) family proteins of proteins (MAGI1, MAGI2, MAGI3) are believed to play a key in cell adhesion by connecting trans-membrane proteins with the cytoskeleton in tight junctions. They have been implicated in the pathogenesis of breast, and gastric cancer. However, their role in human colorectal cancer is less well characterised. In this study, we aim to examine the expression patterns, functions, interactions, and regulatory pathways of MAGI in human colorectal cancer cell lines. **Methods** We have used wild-type human colorectal cancer cell lines (HT115, HRT18, RKO), which have varying invasive properties, with differential expression pattern of MAGI. We examined a panel of ubiquitous cancer cell lines initially, including the aforesaid, for expression of MAGI. We extracted RNA libraries of the aforesaid cell lines, upon which we performed reverse transcription. Levels of the MAGI transcripts in the resulting cDNA were measured by PCR. **Results** Our initial analysis has shown colorectal cancer cell lines (HT115, HRT18, RKO) in specific and other cancer cell lines in general, have positive expression for MAGI1 and MAGI3, but not for MAGI2. **Conclusion** We have some very encouraging results in the initial phase of this study, showing positive expression of MAGI 1 and MAGI 3 in colorectal cancer cell lines. More significantly, we found negligible expression of MAGI2, which has profound implications for any future in vitro studies into its role in human colorectal cancer. Further work is currently carried out on functions, interactions and also regulatory pathways of MAGI in human colorectal cancer cell lines, which shall improve our future understanding of this novel set of proteins.
The role of Activated Leukocyte Cell Adhesion Molecule (ALCAM) in cancer metastasis

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Background Breast cancer is a global health concern accounting for substantial morbidity and mortality. Poor patient prognosis is associated with metastatic dissemination to secondary sites and breast cancer has a predisposition to spread to the bone. Treatment for bone metastasis are limited establishment of these metastasis result in a poor prognosis for the patient. Activated leukocyte cell adhesion molecule (ALCAM) is a member of the immunoglobulin superfamily involved in homophilic (ALCAM-ALCAM) and heterophilic (ALCAM-CD6) binding between cells. ALCAM expression has been found to be dysregulated throughout cancer progression in many different cancer types and differential expression of this molecule has been linked to patient prognosis and likelihood to establish metastatic disease. The current study explores the potential for targeting ALCAM in breast cancer cells and its potential to contribute to the establishment of cells in the bone environment. Methods ALCAM expression was targeted in MDA-MB-231 breast cancer cells using a ribozyme transgene approach. Subsequently, the impact of ALCAM knockdown in vitro was examined through the characterisation of cellular growth, invasiveness, matrix-adhesion and motility. These traits were further examined in the presence of a bone extract and the hepatocyte growth factor (HGF). Results Knockdown of ALCAM in MDA-MB-231 cells significantly reduced cell growth rates and significantly enhanced cell-matrix adhesion. Knockdown of ALCAM also significantly enhanced cell invasiveness and motility. In addition to this, differential effects were seen between the response of control or knockdown cells to HGF and bone matrix proteins. Control cells displayed a greater positive response to both HGF and bone proteins, enhancing both invasion and motility whereas ALCAM suppressed cells did not display such response. Conclusions Taken together our current data suggests that ALCAM plays a role in the regulation of MDA-MB-231 breast cancer cell growth, matrix adhesion, invasion and motility and generally that suppression of ALCAM leads to a more aggressive cell phenotype. Additionally, our data implies that knockdown of ALCAM in MDA-MB-231 cells makes this line less responsive to both HGF treatments and proteins present in the bone environment which can otherwise enhance cell invasion and motility in control cells. Hence ALCAM appears to play a role in governing cell phenotype in the bone environment and may thus be involved in the homing of disseminated cells to the bone.
Percutaneous radiofrequency ablation for medically inoperable patients with clinical stage I non-small cell lung cancer

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Objective Surgical resection is the standard of care for patients with resectable non-small cell lung cancer (NSCLC). However, for high-risk patients radiofrequency ablation (RFA) may offer an alternative option. The purpose of this study was to retrospectively evaluate the feasibility, safety, and effectiveness of percutaneous RFA for medically inoperable patients with clinical stage I NSCLC. Methods Between 2008 and 2014, 29 medically inoperable patients with clinical stage I NSCLC underwent percutaneous RFA by thoracic surgeons. Proof of NSCLC was obtained by biopsy in all patients. Follow-up were scheduled 1 and 3 months after treatment, and then at 3-month intervals for up to 5 years. We evaluated technical success, safety, initial response rate, time to local progression, overall survival and cancer-specific survival. Results Twenty-nine patients underwent CT-guided RFA for medically inoperable patients with clinical stage I NSCLC. There were 18 men and 11 women with a median age of 78.0 years (range 56-85) and mean of 76.0 years. Correct placement of the ablation device into the target tumor with completion of the planned treatment protocol was feasible in all patients. No procedure-related deaths occurred in any of the 33 ablation procedures. Major complications consisted of pneumothorax (n=3), which needed drainage. Minor complications included small pneumothorax in 5, none requiring drainage, chest pain in 8, cough in 1. Side effects (moderate-grade fever <38.5 °C, and/or chest pain) were commonest complications. However, most of them were cured within a couple of days. Complete response was observed in 14.8% of patients, a partial response was observed in 41.4%. Stable disease was noted in 27.6% and progressive disease occurred in 13.8% of patients. The mean follow-up was 25 months. The mean overall survival was 57 months (95% confidence interval of 44-70 months). The mean cancer specific survival was 63 months (95% confidence interval 50-75 months). Overall survival was 90.5%±6.4% at 1 year, 76.4%±10.7% at 2 years, and 65.5%±13.6% at 3 years. Cancer specific survival was 95.2%±4.6% at 1 year, 86.6%±9.3% at 2 years, and 74.2%±13.9% at 3 years in all patients. The survivals for stage IA and IB cancers were 87.5% and 92.3% at 1 year, 87.5% and 73.4% at 2 years, 87.5%, and 58.7% at 3 years, respectively. The survivals were not significantly different between the 2 groups (P=0.596), with mean survival times of 65 months (95% CI: 51–79 months) and 55 months (95% CI: 38–71 months), respectively. Conclusion Our experience indicates that percutaneous RFA done by the thoracic surgeons is safe, feasible and effectiveness procedure in clinical stage I NSCLC with medically inoperable patients who are not fit for surgery.

Keywords: radiofrequency ablation; non-small cell lung cancer; computed tomography
Gastric cancer is associated with increased migration and invasion. In the present study, we explored the role of c-Src in gastric cancer cell migration and invasion. BGC-823 gastric cancer cells were used to investigate migration following treatment of these cells with the c-Src inhibitors, PP2 and SU6656. Migration and invasion were analyzed by wound healing and Transwell assays. Western blot analysis was used to detect the expression of MT1-MMP and VEGF-C, while the activity of MMP2 and MMP9 was monitored with gelatin zymography assay. Immunoprecipitation was used to detect interactions among furin, pro-MT1-MMP and pro-VEGF-C. MT1-MMP and VEGF-C expression levels were inhibited by PP2 and SU6656 treatment, in accordance with decreased c-Src activity. Similarly, the zymography assay demonstrated that the activity of MMP2 and MMP9 was decreased following PP2 or SU6656 treatment. Blockade of c-Src also inhibited the invasive and migratory capacity of BGC-823 cells. Notably, c-Src interacted with furin in vivo, while interactions between furin and its substrates, pro-MT1-MMP and pro-VEGF-C, were decreased by c-Src inhibitors. In conclusion, the interaction among furin and proMT1-MMP or pro-VEGF-C or other tumor-associated precursor enzymes can be regulated by c-Src activity, thus reducing or changing the expression of these enzymes in order to reduce the development of gastric cancer, invasion and metastasis.
Differential expression of serum miR-126, miR-141 and miR-21 as novel biomarkers for early detection of liver metastasis in colorectal cancer

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Objective MicroRNAs (miRNAs) have potential as diagnostic biomarkers in cancer. Evaluation of the association between miRNA expression patterns and early detection of liver metastasis in colorectal cancer (CRC) has not been reported. Methods We investigated the expression of metastasis-associated miRs-31, 335, 206, 141, 126, 200b, 200c, 21, Let-7a, Let-7b and Let-7c in localized, liver-metastatic and other organ-metastatic CRC (OM-CRC). Expressions of target miRNAs in serum were evaluated in 116 consecutive localized CRC (L-CRC), 72 synchronous liver-metastatic CRC (SLM-CRC) and 36 other OM-CRC by quantitative real-time PCR. Results Seven of 11 tested miRNAs could be detected from serum. Four miRNAs, miR-126, Let-7a, miR-141 and miR-21 were identified as metastasis-associated miRNAs. Compared with L-CRC, significant upregulated expression was observed for miR-141 and miR-21 in SLM-CRC and OM-CRC, down-regulated expression was observed for miR-126 in SLM-CRC and OM-CRC, and up-regulated expression of Let-7a in OM-CRC. The receiver operating characteristic (ROC) curve showed serum miR-126 had a cut-off [log10relative quantity (log10RQ)= −0.2005] with 77.78% sensitivity and 68.97% specificity with an area under curve (AUC) of 0.7564, miR-141 had a cut-off (log10RQ= −0.2285) with 86.11% sensitivity and 76.11% specificity with an AUC of 0.8279, and miR-21 had a cut-off (log10RQ= −0.1310) with 73.61% sensitivity and 66.38% specificity with an AUC of 0.7479. Conclusions We identified liver metastasis-associated miRNAs, suggesting serum miR-126, miR-141 and miR-21 may be novel biomarkers for clinical diagnosis of early stage liver-metastatic CRC.

【Keywords】MicroRNA (miRNAs); colorectal cancer (CRC); liver metastasis; diagnosis
The prognosis of gastric cancer (GC) is associated with Cdx2 and nuclear PTEN coexpression. This study aimed to determine the expression patterns of Cdx2 and PTEN in various GC tissues and cell lines to identify their relationship in GC. Immunohistochemistry was undertaken to assess the expression patterns of Cdx2 and PTEN in paraffin-embedded specimens of 228 GC patients who had undergone radical D2 gastrectomy with long-term follow-up. Cell growth and tumorigenicity were analyzed in the BGC823 cells with exogenous Cdx2 and any changes in the associated signaling pathways were interpreted in exogenous cdx2 expression and cdx2 knockdown. Cdx2 was found in the nuclei of GC cells in 43.4% (99/228) of the paraffin-embedded biopsies. A higher expression of nuclear PTEN was observed in 36.4% (83/228). Coexpression of Cdx2 and nuclear PTEN was detected in GC tumors (59/228, 25.9%) which correlated with the prognosis of advanced GC patients (p<0.001). The expression levels of Cdx2 and PTEN were variable in the different GC cell lines. However, the trends were similar between PTEN and Cdx2 in GC tissues and cell lines. High expression of Cdx2 and PTEN significantly reduced tumorigenicity in BGC823 cells compared with the empty vector control. Exogenous expression of Cdx2 triggered the upregulation of PTEN expression and decreased PI3K and pAkt expression and vice versa. The coexpression levels of PTEN and Cdx2 in GC tumors correlated with prognosis in GC patients. Cdx2 may play a role in the upregulation of PTEN by triggering PI3K/Akt inactivation in GC cells.
S100P enhances the chemosensitivity of human gastric cancer cell lines

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Background The effect of the protein S100P on biological characteristics of cancer is not clear, especially in gastric cancer. We previously showed that S100P positive gastric cancer patients have a better cumulative survival than S100P negative patients. Objective To study the possible mechanisms of S100P enhanced the chemosensitivity to oxaliplatin in gastric cancer cell lines. Methods S100P was overexpressed in vitro by plasmid transfection and downregulated by siRNA transfection in the BGC823 and SGC7901 gastric cancer cell lines. Cell survival rate, changes in the chemoresistance gene, such as GST-x, MDR1, MRP1, Topo-II, MVP and BCRP, and intake of anticancer drug were measured after oxaliplatin treatment. Results In SGC7901 cells, MTT assay indicated that increased S100P expression levels decreased the survival rate and decreased S100P expression levels increased the survival rate. In BGC823 and SGC7901 cell lines, mRNA of MDR1, a chemoresistance gene, was decreased in cells that overexpressed S100P, and increased in cells with downregulation of S100P. Intracellular accumulation of platinum increased in cells with overexpressed S100P, and decreased in cells with S100P downregulation. Conclusions S100P contributes to oxaliplatin chemosensitivity in gastric cell lines by increasing drug inflow. It might also be a novel independent prognostic factor in gastric cancer patients who receive adjuvant chemotherapy with oxaliplatin.

【Keywords】S100P; oxaliplatin; gastric cancer; chemosensitivity
Vascular endothelial growth inhibitor affects the invasion, apoptosis and vascularisation in breast cancer cell line MDA-MB-231

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Background Breast cancer is one of the most common malignant female diseases worldwide. It is a significant threat to every woman’s health. Vascular endothelial growth inhibitor (VEGI) is known to be abundant in endothelial cells. According to previous literature, overexpression of VEGI has been shown to inhibit tumor neovascularisation and progression in cellular and animal models, but there has been limited research on the significance of VEGI in the breast cancer. Methods In our study, cell lines MDA-MB-231 were first constructed in which VEGI mediated by lentivirus over-expressed. The effects of VEGI over-expression on MDA-MB-231 cells were investigated both in vitro and in vivo. The expression of VEGI in the MDA-MB-231 cells after infection of lentivirus was analyzed using real-time PCR and Western blotting. The effect of the biological characteristics of MDA-MB-231 cells was assessed by growth, invasion, adhesion, and migration assay with subcutaneous tumor-bearing nude mice models. Then the growth curves of the subcutaneous tumors were studied. Expressions of VEGI, CD31, and CD34 in the tumors were analyzed by immunohistochemistry and apoptosis was detected by flow cytometry and immunohistochemistry. Results Infection of MDA-MB-231 cells with the lentivirus resulted in approximately a 1000-fold increase in the expression of VEGI. As seen in the invasion, adhesion and migration assay, the over-expression of VEGI can inhibit the ability of MDA-MB-231 cells during migration, adhesion and invasion. The volume of the subcutaneous tumor in the over-expression group was distinctly and significantly less than that of the control groups. Immunohistochemistry analysis of the tumor biopsies clearly showed the expression of VEGI in the over-expression group increased while CD31 and CD34 decreased significantly. In vitro and in vivo, the early apoptosis rate and the apoptosis index were increased within the VEGI over-expression group as compared with the control group. Conclusions Taken together, recombinant lentivirus that was successfully constructed, demonstrated up-regulated VEGI gene expression in breast cancer cells. Lentivirus-mediated over-expression of VEGI weakened the ability of the breast cancer cell migration, adhesion and invasion. Over-expression of VEGI diminished the tumorigenic capacity of breast cancer cells in vivo. Up-regulation of VEGI gene expression however inhibited breast cancer MDA-MB-231 cell in the early apoptosis.

Keywords breast cancer; lentivirus; MDA-MB-231; apoptosis
An anatomical, histopathological, and molecular biological function study of the fascias posterior to the interperitoneal colon and its associated mesocolon: their relevance to colonic surgery

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The study aim was to explore the anatomy, histopathology, and molecular biological function of the fascias posterior to the interperitoneal colon and its mesocolon. We performed intraoperative observations in 60 interperitoneal colon-cancer patients accepted for complete mesocolic excision and conducted local anatomy observations for five embalmed cadavers. An additional two embalmed child cadaver specimens were studied with large slices and paraffin sections. Ten of the 60 patients were examined with a lymph node tracer technique in vivo, while fresh specimens from these patients were assessed by histopathological examination and transwell cell migration assays in vitro. The anatomical and histopathological findings showed that the fascias posterior to the interperitoneal colon and its associated mesocolon were composed of two independent layers: the visceral and parietal fascias. These two fascias were primarily composed of collagen fibers, with the parietal fascia containing a small amount of muscle fiber. The in vivo test showed that the visceral fascia surrounded the colon and its associated mesocolon, including vessels and lymphatics, and that it had no lymphatic flow through it into the rear tissues. Moreover, the in vitro assays showed the visceral fascia was able to block tumor cell migration.
Comparison of metastatic lymph node ratio staging system with the 7th AJCC system for colorectal cancer

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Purpose To evaluate the prognostic value and staging accuracy of the metastatic lymph node ratio (rN) staging system for colorectal cancer. Methods A total of 1,127 patients with colorectal cancer who underwent curative surgery between 2000 and 2011 at our institute were analyzed. Lymph nodes status was assigned according to AJCC pN system and rN system. Patients with colon cancer (group 1, n = 652) and rectal cancer (group 2, n = 475) were analyzed separately. Results The rN staging system was generated using 0.2 and 0.6 as the cutoff values of lymph node ratio and then compared with AJCC pN stages. Linear regression model revealed that the number of retrieved lymph node was related to number of metastatic lymph nodes. After a median follow-up of 46 months, the 5-year survival rates of patients with more than 12 lymph nodes (LNs) retrieved were better than cases with fewer than 12 LNs, while the differences were not obvious in rN classification. Conclusions The rN category is a better prognostic tool than the AJCC pN category for colorectal cancer patients after curative surgery.
Both macrophages and hypoxia play critical role in regulating invasion and metastasis of gastric cancer

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Background Macrophages play an important role in the link between chronic inflammation and cancer. As previously demonstrated, tumor associated macrophages (TAMs) infiltration is associated with some cancers invasion and metastasis. However, the role of TAMs in the gastric cancer remains unclear. Methods Three dimensional dynamic migration imaging system and real-time RT-PCR were used to quantitatively investigate the effect of macrophages on the cancer cell mobility and gene expression related to cancer invasion and metastasis, including ADAM8, ADAM9, MMP9, TIMP3, VEGF-1, and IL-8 genes, in AGS, HGC-27, Hs-746T, and NCI-N87 gastric cancer cell lines under normal or hypoxic conditions. Results Under normal conditions, the cancer cell mobility was increased significantly and all six gene expressions were up regulated in all four cancer cell lines by macrophages. Under hypoxic conditions, the increase in the migration rate induced by macrophages was decreased in HGC-27 and Hs-746T cell lines, which also showed increased TIMP3 expression as compared to normal conditions with macrophages. In AGS cell line, the increase in migration rate induced by macrophages was further elevated under hypoxia with increased ADAM8 and ADAM9 expression and decreased MMP9 and TIMP3 expressions. Under hypoxia, the induction by macrophages for IL-8 expression was increased significantly in NCI-N87 cell line and VEGF-1 was increased in HGC-27 cell line. Conclusion Both macrophages and hypoxia play an indispensable role in regulating the invasion and metastasis of gastric cancer. The effect of hypoxia on TAMs depending on cell lines might provide new opportunities for improving gastric cancer treatment with macrophages through changing the oxygen condition based on tumor individual characteristics.
Vasohibin-1 plays an important role in invasion and metastasis of colorectal cancer as an angeogenesis inhibitor

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Background Vasohibin-1 has been recently identified as a negative feedback regulator of angiogenesis. However, the expression of vasohibin-1 in colorectal cancer and its correlations with VEGF-A, microvessel density (MVD) and the prognosis of the patients remain unclear. Materials and methods Vasohibin-1 and VEGF-A expression were measured in 132 paraffin-embedded tissues of colorectal cancer by immunohistochemistry and Western blot, as well as in colon cancer cell lines and normal colon cell by Western blot and q-PCR. MVD was measured by counting CD34 positive clusters in a single field of view with the most intensive neovascularization of colon cancer tissues. Correlations between expression of Vasohibin-1, VEGF-A, MVD, clinicopathological features, and prognosis were analyzed. Results Vasohibin-1 and VEGF-A proteins were expressed in 88.64% and 84.09% colorectal cancer tissues, respectively. Positive correlations were found between vasohibin-1, VEGF-A expression, and MVD. Vasohibin-1 expression has significant positive correlation with pathological TNM stage, tumor stromal invasion, lymph node status, and distant metastasis. Patients with high vasohibin-1 expression had significantly worse overall survival and progression-free survival than those with low expression. Conclusion Vasohibin-1 is a clinically relevant predictor of patient prognosis in colorectal cancer and might become a new biomarker in patients with colorectal cancer.
A preliminary screening of differentially expressed miRNAs between cancer and adjacent tissues of esophageal squamous cell carcinoma

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Objective To screen the differential expression profiles of microRNAs (miRNAs) between cancer and adjacent tissues of esophageal squamous cell carcinoma (ESCC) patients in Linzhou city, Henan province, and provide basis for further confirming ESCC-related miRNAs and the mechanism researching of ESCC. Methods Cancer and adjacent tissues from 4 patients with newly diagnosed ESCC were obtained. MiRNAs were determined by high-throughput miRNA microarray. Results Among the 1888 human relevant miRNAs probes detected by miRNA microarray, there were 38 differentially expressed miRNAs between esophageal cancer tissues and tissues adjacent to the tumors (P<0.05), including 17 overexpressed miRNAs and 21 under-expressed miRNAs. Conclusion There may be relationship between the profile of differentially expressed 38 miRNAs and the occurrence and development of ESCC, and we still need to verify the result in a larger population.

Keywords: esophageal squamous cell carcinoma; microRNA; array; differential expression
Video-assisted thoracic surgery for 120 patients with solitary pulmonary nodules

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Objective To investigate the diagnosis and surgical treatment of solitary pulmonary nodules (SPN). Methods 120 cases of SPN-resection patients (73 male, 47 female) in our hospital, from January 2006 through June 2012, were retrospectively analyzed. All cases were confirmed by chest CT scan, 82 cases of peripheral lung nodules, 38 cases near the lung hilum. Simple excision in 22 cases, wedge resection in 57 cases, segmental resection in 9 cases, lobectomy in 32 cases. Results Postoperative pathology confirmed malignant nodules in 78 cases (65%), including 51 cases of primary lung cancer, non-small cell lung cancer (39 cases), pathological stage: IA (T1N0M0) 19 cases, IIA (T1N1M0) 9 cases, IIIA (T1N2M0) 11 cases; 27 cases of metastatic tumor, 42 cases of benign nodules (35%). In larger than 1.0 cm in diameter, solid and subsolid nodules were 72.9% (70/96 cases), 73.1% (57/78 cases) and 50% (21/42 cases) respectively. The sensitivity of CT diagnosis of malignant SPNs was 71.8% (56/78), the specificity was 33.3% (14/42); PET-CT sensitivity and specificity was 93.4% (57/61) and 76% (19/25). The sensitivity and specificity of percutaneous lung puncture biopsy was 92.8% (64/69) and 100% (13/13), respectively. Conclusion The SPNs imaging features play an important role in the judgment of clinicians. The risk factors of diameter greater than 10 mm, the SPN should take corresponding examination, diagnosis, and treatment measures.

Keywords video-assisted thoracic surgery; solitary pulmonary nodule; diagnosis; treatment
Are endothelial cell tight junctions a key mechanism in the prevention of brain metastasis?

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The interaction and penetration of endothelium by the metastasising tumour cell is a key step in the formation of metastasis. Metastatic brain tumours are frequently observed in patients with lung, breast and malignant melanoma and so brain metastasis (BM) remains a significant clinical issue. The blood brain barrier (BBB) is maintained and regulated by Tight Junctions (TJs).

Therefore a key step in the penetration of the BBB by cancer cells is their interaction with the endothelial cells of the BBB and the disruption of the TJ between them. As our knowledge and understanding of the molecular structure, mechanism of action and function of TJs is expanded the TJ can be regarded as a potentially important target for anti-cancer research and a possible area for future therapeutics.

We will examine the role of the TJ in the endothelia and how this translates to interaction with cancer cells during cancer metastasis. We will then focus on the endothelial cells that constitute the BBB. Factors that affect the structure and function of TJ will be discussed.
**Major Organizers**

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Cancer Institute of Capital Medical University

Beijing Lung Cancer Centre, Capital Medical University

Department of General Surgery, Capital Medical University

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Basic Medical School of Capital Medical University

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Beijing Key Laboratory of Cancer Invasion & Metastasis Research

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