

赵玉沛: 北京协和医院院长,著名外科学教授,博士生导师。在肝胆、胃肠、甲状腺等普外领域进行了许多开创性工作,尤其对胰腺外科有着深厚的造诣,对胰腺癌等疾病进行了系统性的基础与临床研究,取得了丰硕成果。

按语:转化医学是近10年来国际医学健康领域出现的新概念,它能够打破基础医学与药物研发、临床医学之间固有的屏障,建立起彼此的直接关联,缩短从实验室到病床应用的过程。本文重点介绍了北京协和医院转化医学研究的发展历史及今后的发展方向。建立了三个转化医学的切入点,即胰腺疾病、肺及呼吸系统疾病和代谢疾病。读者通过本文将了解到成熟的转化医学体系必将能引领我国未来医学发展之路朝着普惠化、规范化和预防性、预测性、个体化及参与性的方向前进。

转化医学在协和:过去、现在与未来



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转化医学是近 10 年来国际医学健康领域出现的新概念,它能够打破基础医学与药物研发、临床医学之间固有的屏障,建立起彼此的直接关联,缩短从实验室到病床应用的过程。转化医学将科研机构获得的研究成果,经过快速验证,最终以产品的形式转化为临床上的诊断和治疗新方法,让患者更快受益于医学、生物乃至机械信息等科技。因此转化医学得到了各国政府和学术机构的广泛重视。

实际上,转化医学的概念虽然是新的,但内容并不是新的。老协和就是中国"转化医学"的摇篮之一,从她建立伊始,就强调在基础与临床研究之间进行转化,并在很多研究领域卓有建树,她为中国培养了众多的医学大师,他们是我国转化医学最早的开拓者和践行者。

早在上世纪中叶,协和生化系吴宪教授就对生物化学与临床医学的联系进行了深入研究和精辟阐述,根据他于1919年提出的"血液系统分析法",能制备出无蛋白质的血液,使血液中重要成分,如氨基酸,肌酸,肌酸酐,尿素,非蛋白氮,以及血糖,乳酸等得以测定出来。1929年在波士顿召开的第13届国际生理学会上他提出蛋白质变性学说:认为天然蛋白质分子不是一长的直链而是一紧密的结构。这种结构是借肽键之外的其他键,将肽链的不同部分连接而形成的,所以容易被物理及化学的力所破坏,即从有规则的折叠排

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列形式变成不规则及松散的形式。这个学说对于研究 蛋白质大分子的高级结构有重要价值。1927年,他 开始研究中国人的营养问题,着重阐明了素膳与荤膳 的优缺点,并于1938年制定了《中国民众最低限度 之营养需要》标准。他在临床化学,蛋白质化学, 免疫化学以及营养学等领域都有许多创见和论述。 他的血液系统分析法至今一直在临床诊断方面起着 重要作用。

刘士豪教授是我国著名的内分泌专家, 他既是协 和医学院生物化学系教授, 又是协和医院内分泌科的 临床医师。他毕生致力于中国内分泌学科的建立和发 展,做了许多开拓性的工作,他很早就认识到内分泌 学无论在临床医学或是基础医学中, 都占有十分重要 的位置。20世纪30年代即在协和医院首建代谢病房 和相应的实验室。1965 年,他首次在中国建立了胰 岛素放射免疫及醛固酮的测定方法。刘士豪教授一生 中最重要的贡献就是对钙磷代谢的研究,他与内分泌 专家朱宪彝合作研究"骨软化症的钙磷代谢",对肾 性骨营养不良、纤维性胃炎、败血症的钙磷代谢进行 了深入的研究,发表论著 17 篇;他于 20 世纪 30~ 40 年代证明了骨软化症的主要原因是维生素 D 缺 乏,在国际上首次证实维生素 D 可通过母乳治愈婴 儿佝偻病,并首次运用双氢速变固醇治疗肾性骨营 养不良症。

林可胜是在国际上享有盛誉的生理学家,他致力于痛觉生理和镇痛药物的研究,是中国早期能开展高水平科学研究的为数极少的科学家之一,对消化生理学与痛觉生理学均有超越前人的卓越奉献。他在国际上首先设计和进行了有效区分外周镇痛和中枢镇痛的药物药理科学实验,证明了阿司匹林能阻断传递痛觉的感觉神经末梢的冲动发生,从而揭示了阿司匹林在外周发挥镇痛作用的原理。在实验中,他曾把缓激肽注入自己的动脉,再用阿司匹林来缓解由此产生的身体的剧烈疼痛,亲身感受阿司匹林镇痛的过程和原理。林可胜在医学上开创性的研究得到全球医药卫生界的推崇,他所进行的关于阿司匹林镇痛机理的科学实验至今仍被诺贝尔奖得主、英国科学家维恩爵士誉为经典工作。

新中国成立后,协和人秉承老协和精益求精,孜 孜不倦的精神,始终将转化医学的理念贯穿于整个科 研及医疗工作中。现在北京协和医院是国家疑难重症 诊治中心之一,现拥有一级学科博士授权点3个,二 级学科博士授权点14个,硕士授权点21个;拥有博

士生导师104人、硕士生导师206人。医院现有中国 科学院院士1人,中国工程院院士3人,国家级、部 级"有突出贡献中青年专家"17人,享受政府特殊 津贴 150 人。协和拥有大量的临床信息和生物标准 库,拥有最好的临床专家队伍和最先进的技术设备, 可整合、共享医科院多家院所的优势资源,拥有与国 际接轨的临床药理基地、卫生部内分泌重点实验室、 医学分子生物学国家重点实验室以及国家级医学、生 物医学信息中心图书馆。以上为协和转化医学中心的 成立奠定了坚实的基础。协和也为成立转化医学中心 做了多项准备。自2007年起,协和医院与医科院基 础医学研究所先后联合举办了"基础与临床论坛"、 "转化医学研究课题"和"转化医学研究沙龙"。成功 举办了多次"协和转化医学论坛"及"中美临床与转 化医学研究国际论坛"。2010年9月16日,北京协和 医院正式成立了包括54位院士加盟的以医院为依托, 以现有转化医学研究的条件为基础的转化医学研究平 台——协和转化医学中心。中心在成立伊始就深刻的 认识到转化医学不仅是一种理念, 更是一种行动。转 化医学就是要从临床重大需求出发,凝练科学问题, 通过基础和临床研究,找到解决问题的方法,提高诊 断、治疗和预防水平。协和转化医学中心的发展目标 是成为国家级的转化医学中心,这正像协和医院建立 时的目标一样,要成为中国乃至世界最好的医院。其 次,协和转化医学中心的研究平台是以临床研究所为 核心的,整合内部多个部门并联合国内多家科研机构 开展研究工作。为了使协和转化医学中心具有高起 点,我们还专门聘请了国内顶尖专家学者组成咨询机 构,并设立单独的工作机构。

协和转化医学中心将实施海内外高端人才的双聘、特聘制度,建立与国内外高水平机构间的交流互访和资源共享机制;同时采取统筹管理与协调、开放流动的运行机制,先在医科院系统整合和转化,进行不同模式转化研究的探索和尝试。从基础到临床,把现有基础医学及药物研究优势资源及其研究成果,快速转化和应用;从临床(发现问题)到基础(采用先进的分子生物学技术和动物模型等进行深入研究),再到临床(临床试验),共同解决临床中亟待解决的问题。同时,协和转化医学中心还将发挥北京协和医院丰富的病例、临床专家队伍和先进的技术设备等资源优势,努力建成国家级、国际化的转化医学研究合作高端平台。

未来协和转化医学中心开展转化医学研究将从以

下几个方面人手:即培养专门的人才、筹措充足的资 金、建立组织标本库和病人数据库、建立完备的体系 和适合实际情况的线路图及整体规划。首先, 培养专 门的转化医学人才是转化医学事业可持续发展的关 键, 因此协和转化医学中心除了吸引外来优秀人才以 外, 更要尝试建立人才培养机制, 使一部分临床人员 成为研究型医生或研究型护士。其次,开展转化医学 事业需要大量的资金,目前国内转化医学研究的资金 主要来自医疗机构本身和国家投入,制药企业与民间 资本的参与较少。应建立一种联系机制,整合各种资 金链,除了向政府部门申请资金支持外,还要拓展渠 道,争取来自医药企业和民间的资金,让社会各界特 别是工业界广泛参与转化医学研究。第三,建立开展 转化医学研究的基础平台,特别是全国性的人体组织 标本库、患者信息库和健康人电子医学档案。第四, 建立完备的体系, 重点搭建全国性的转化医学研究平 台。从2009年至今,国内成立了近40家各种类型的 转化医学中心。从积极的角度评价、说明我国转化医 学事业蓬勃发展,学术界对转化医学给予厚望,具有 缺少整体规划,随便挂牌,彼此冲突、交叉,处于一 这次浪潮中定能够大有可为。

种"割据"状态。其结果必然是资源浪费、重复研 究、效率低下、孤军奋战。因此, 协和将努力建成国 家层面的转化医学研究中心,整合国内现有转化医学 资源, 再辐射周边城市和研究机构。第五, 制定符合 实际情况的线路图。协和转化医学中心目前的重点扶 持对象是常见病和罕见病, 现已建立了三个转化医学 的切入点,分别是胰腺疾病、肺及呼吸系统疾病和代 谢疾病。将来再根据情况逐步铺开,扩大转化医学事 业的研究面。

经过几代协和人的不断努力, 转化医学事业已经 在协和落地、生根、发芽, 现在正不断的茁壮成长, 相信未来能够更加繁荣,取得丰硕的成果。而我国要 想实现全民健康计划、提高全体国民的健康水平, 必 须要大力开展转化医学研究, 让基础医学和临床医学 研究者联手, 在转化医学平台的基础上开展研究, 并 将研究成果工业化,最后应用到个体和人群中,提高 国民的健康意识和健康水平, 最终形成良性循环。相 信一个成熟的转化医学体系必将能引领我国未来医学 发展之路朝着普惠化、规范化和预防性、预测性、个 浓厚的兴趣;但是另一方面,也说明我国的转化医学 体化及参与性的方向前进。相信协和转化医学中心在 Translational Medicine Research (Electronic Edition), 2011, 1 (2): 1-7





Yu-pei Zhao, president of Peking Union Medical College Hospital, the famous professor of surgery, doctoral tutor. He has done a number of pioneering work in the liver, thyroid, gastrointestinal surgery area, especially in pancreatic surgery, he has systematically developed the basic and clinical research on pancreatic cancer and get fruitful results.

Editorial note: Translational medicine is an emerging field for international medical researchers in the past 10 years breaking inherent barriers between basic medicine and drug development, as well as clinical medicine, thereby establishing a direct link between these different fields shortening the processes from research laboratory to clinical application. This article introduced the history and future direction of Translational Medicine Research of Peking Union Medical College Hospital (PUMCH). PUMC Translational Medicine Center currently focuses on common and rare diseases and has found 3 points of penetration in translational medicine, namely, pancreatic disease, lung and respiratory diseases and metabolic diseases. Readers will understand the that an efficient, mature translational medical system can competently lead China's medical field toward a more universal, beneficial, and standardized direction which will provide better prevention and prediction bringing health benefits to more people.

Translational medicine at Peking Union Medical College (PUMC): past, present and future

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Translational medicine is an emerging field for international medical researchers in the past 10 years breaking inherent barriers between basic medicine and drug development, as well as clinical medicine, thereby establishing a direct link between these different fields shortening the processes from research laboratory to clinical application. Translational medicine involves verification and transformation of laboratory findings into new ways for diagnosis and treatment, thus benefitting patients with medical, biological, pharmacological mechanics and information technology. Therefore, translational medicine has drawn wide attention of governments and academic institutions of many countries, worldwide.

The concept of translational medicine is new, while in fact, the focus of which is not. The former Peking Union Medical College (PUMC) is deemed to be one of the cradles of "Translational Medicine" in China, and since its establishment PUMC began to emphasize on translation between basic and clinical research, making major contributions in many fields. PUMC has cultivated a large number of great masters in medical fields for our country, who were the earliest pioneers and practitioners in translational medicine in China.

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In the middle of the last century, Professor Xian Wu of Biochemistry Department of PUMC, performed penetrating and intensive researches on the relationship between biochemistry and clinical medicine proposing the "Blood System Analysis" in 1919. He postulated, according to which, protein-free blood could be prepared and the important components of blood (such as amino acids, creatine, creatinine, urea, non-protein nitrogen, glucose and lactic acid) could be detected. Besides the Blood System Analysis Professor Xian Wu also proposed the theory of protein denaturation during the IUPS 13th World Congress in Boston in 1929 in that natural protein molecule is not a long straight-chain, but a tight structure. A molecular structure formed by a connection of different sites of peptide chains via other linkages rather than only peptide linkage, causing the structure to be easily broken by physical and chemical forces changing from a regular folded type of arrangement to an irregular and loose format. This theory had important value in study on advanced structure of large protein molecules. In 1927, Professor Xian Wu began to study Chinese people's nutrition highlighting the advantages and disadvantages of vegetarian diet and meat diet in which he formulated Minimum Nutritional Requirements for Chinese People. He also developed numerous other creations and discussions in clinical chemistry, protein chemistry, immunochemistry, nutrition and related fields.

Professor Shihao Liu a renowned endocrinologist in China and a Professor in Biochemistry and a clinical physician in Endocrinology in PUMC devoted his life's work to the establishment and development of endocrine disciplines in China having completed much of the pioneering work in this field. Professor Liu recognized that endocrinology plays a very important role in both clinical medicine and basic medicine. He first established metabolic wards and a laboratory at PUMC early in the 1930's. In 1965 he first established insulin radio immunoassay and aldosterone assay in China. Shihao Liu's most important contribution was the study on calcium and phosphorus metabolism and partnering medical expertise with endocrinologist Xianyi Zhu. Together they performed studies on "calcium and phosphorus metabolism in osteomalacia", penetrating researches on renal osteodystrophy, fibrous gastritis, calcium and phosphorus metabolism of sepsis with 17 papers published. During the 1930s and 1940s, Professor Shihao Liu proved that osteomalacia was mainly caused due to vitamin D deficiency, internationally confirmed for the first time that vitamin D can cure rickets among infants through breast milk and first applied dihydrotachysterol for the treatment of renal osteodystrophy.

Kesheng Lin a renowned worldwide physiologist had committed himself to algesic physiology and analgesics research. He was one of very few scientists who could conduct high-level scientific research early in China making outstanding contribution to digestive physiology and algesic physiology. He was the first scientist who designed and conducted scientific experiments internationally which effectively distinguished pharmacology between peripheral and central analgesic drugs, and proved that aspirin could block impulses of sensory nerve endings which transmit pain, so as to reveal the peripheral analgesic principle of aspirin. He once injected bradykinin into his own artery and then used aspirin to relieve the resulting pain for experiencing the process and the principle of aspirin's analgesic effects. His creative researches in medical fields had been highly praised by global medical and health authorities. Kesheng Lin's scientific experiments on aspirin analgesic mechanism were considered as classic work by Wilhelm, both a Nobel Prize winner and British scientist.

After the founding of New China, the PUMC adhered to the essence of "Keep improving, and study tirelessly" and had been applying concepts of Translational Medicine throughout their scientific and medical researches. Currently, PUMC is one of National Treatment Centers for Complicated Diseases with 3 Class -1 discipline doctor degree authorization programs, 14 Class -2 discipline doctor degree authorization programs, 21 master degree authorization programs, 104 doctoral supervisors, 206 master tutors, 1 academician with Chinese Academy of Sciences, 3 academicians with Chinese Academy of Engineering, 17 young experts with outstanding contributions (both national and ministerial) and 150 elite personnel with special government allowances. PUMC has the access to a large amount of clinical information and a biological standard library, a team of the best of clinical experts, the most advanced technology and equipment and the ability to integrate, share medical advantages of resources from numerous medical institutes. PUMC has its own internationally integrated clinical pharmacology base, key endocrine laboratories with the Ministry of Health, key Medical Molecular Biology State Laboratory and National Medical and Biomedical Information Center Library. These facilities provide a solid base for the establishment of Translational Medical Center within PUMC allowing adequate preparation to establish a fully functional Translational Medical Center.

Since 2007, PUMC, cooperating with the Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences has successively organized "Basic and Clinical Medicine Forum", "Translational Medicine Research" and "Translational Medicine Research Salon" as well as a

series of "PUMC Translational Medicine Forum" and "Sino-US Clinical and Translational Medical Research Forums" . On September 16, 2010, PUMC Hospital officially formed the translational medical research platform (i. e. PUMC Translational Medicine Center) involving 54 academicians based in hospitals and existing medical research institutions. The Center has been recognized that Translational Medicine is not only a concept, but requires practical actions. The aim of Translational Medicine is to thoroughly analyze scientific issues with the view of major clinical demands, try to apply basic and clinical medicine in resolving problems, improving diagnosis, treatment and prevention. The development objective of PUMC Translational Medicine Center is to become a national Translational Medicine Center consistent with the establishment objective of PUMC Hospital to become one of the best hospitals in China and internationally as well. Furthermore, the study platform in PUMC Translational Medicine Center is centering on clinical research, integrating many internal departments and carrying on researches in cooperation with several research institutions across the country. PUMC Translational Medicine Center has gathered a group of top experts from medical fields to form an advisory body and set to work independent operation mechanisms in order to provide a high starting point for the Center.

The PUMC Translational Medicine Center will establish a Bilateral Contractual Employment and Special Employment system to attract outstanding Chinese talent and other countries setting up a mutual exchange and resource sharing mechanism with national and international high-level institutions. In the interim, the Center will apply overall management and coordination opening a mobile operating system to realize integration among different Institutes of Medical Science performing translational trials and research by using different modes while rapidly transferring and applying available achievements that resulted from basic medicine and drug research. Moreover PUMC will realize translation from basic medicine (identify problems) to clinical medicine (perform further research via advanced molecular biology techniques and animal models), then back to basic medicine (clinical trials) to solve major problems in clinical practice. Beijing PUMC Translational Medicine Center will make good use of abundant medical cases, clinical specialists, advanced technology and equipment and other resources to establish a national and international high-level medical research platform.

The foreseeable future will see PUMC Translational Medicine Center carry out translational medical research from the following aspects: Training specialized personnel, raising sufficient funds, establishing tissue sample bank and patient database, setting up a fully operational system through practical situations and overall planning.

The first key point is training specialized medical personnel to promote sustainable development of Translational Medicine, thus PUMC Translational Medicine Center will not only attract talent from China and other countries but also try and set up a personnel training system schooling part of the clinical research staff into becoming investigative doctors and nurses.

Secondly, development of Translational Medicine requires financial support. Current funding used is mainly from the medical institutions and national investment, while little comes from pharmaceutical companies and little non-governmental capital. Thus, a liaison mechanism should be established integrating various financial chains, to acquire financial support via other approaches such as pharmaceutical companies and non-governmental capital in addition to Government investment. This will promote various business communities to participate in research in Translational Medicine, especially from the industrial sector.

Thirdly, to establish primary platforms for Translational Medical research especially through the National sample bank of human tissues, patient database and electronic medical files of healthy people.

Fourthly, a complete system shall be established to focus on national platforms for Translational Medical research. Forty different types of translational medicine centers have been established since 2009. Evaluating this from a positive view point, China sees vigorous development of Translational Medicine, with excellent expectations anticipated and interest shown in Translational Medicine by various academic circles. But on the other hand, rapidly emerging of these centers indicates a lack of overall planning for Translational Medicine, an aspect that allows inexact, conflicting, and overlapping conditions placing this medical discipline into a "isolated" field. Allowing this to happen will lead to a waste of resources, duplication of research, low efficiency, and disunity. The PUMC is therefore attempting to build Translational Medical Research Centers on national levels, to integrate the currently available domestic resources in this field and then to involve the surrounding cities and research institutions.

Fifthly, formulate a practical program. PUMC Translational Medicine Center currently focuses on common and rare diseases and has found 3 points of penetration in Translational Medicine, namely, pancreatic disease, lung and respiratory diseases and metabolic diseases. The Center will expand the disease range depending on

the situation gradually enlarging research on Translational Medicine.

After combined efforts of several generations, Translational Medicine retained its status steadily at PUMC, taking roots, sprouting and keeping growing and we believe that PUMC will make greater progress and prove further success in this medical field. Now, penetrating research on Translational Medicine should be widely carried out in China by integrating basic medicine and clinical medicine further achieving universal health programs thereby improving the wellbeing level of all citizens.

Translational Medicine industrializes research achievements which will eventually be applied to the whole population contributing to the improvement of health awareness levels of the people forming a virtuous circle. We believe that an efficient, mature Translational Medical system can competently lead China's medical field toward a more universal, beneficial, and standardized direction which will provide better prevention and prediction bringing health benefits to more people. Furthermore we expect that PUMC Translational Medicine Center can make greater contributions in this specialized field.