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Editorial

Gendicine: The First Commercial Gene Therapy Product

I recently returned from a 2-week tour of Asia, where I visited a number of universities in Taiwan, Hong Kong, and mainland China. During this trip I had the opportunity to interact with a number of faculty and students. The most vivid impressions came from my visits to universities in the Chinese cities of Guangzhou, Chengdu, and Shanghai. The growth of these cities and the establishment of new infrastructure were absolutely amazing—cranes jutted into the sky everywhere I looked. The students insisted I give my lectures in English without translation and they engaged in very active and insightful debate about the science of gene therapy. Every hospital I visited had, or was developing, translational research programs to facilitate the creation and evaluation of gene therapies for a wide variety of diseases, with a particular emphasis on cancer. Many of these programs were quite sophisticated and were advancing into clinical trials.

One area that I was keen to learn more about was the biologic agent, called Gendicine, that the Chinese company Shenzhen SiBiono GeneTech (Shenzhen, China) was distributing as the first commercially approved gene therapy product. This product, based on an adenovirus serotype 5 vector engineered to express p53, was approved by the State Food and Drug Administration of China (SFDA) for treatment of patients with head and neck squamous cell carcinoma (HNSCC). As of July 31, 2005, Gendicine has been used to treat more than 2600 patients, with a projected 50,000 patients to receive this product by 2006 (Dr. Zhaohui Peng, unpublished data). This product is in late-stage clinical trials for a variety of other malignancies, as well.

The international gene therapy community has watched the evolution of gene therapy research in China and the development of the first commercial product with mixed emotions. Broad-based support for the field, irrespective of where it occurs, is a plus. In addition, we all will benefit from clinical successes. However, I have heard concerns about the robustness of the regulatory process for approval of new therapies and the willingness of the scientists to share data relevant to the evaluation of this product. In fact, much of the clinical data are published in the Chinese literature, which, unfortunately, is not easily accessed by scientists in the West. With this in mind, I asked Dr. Zhaohui Peng, the CEO of SiBiono GeneTech, to write a review summarizing the key clinical data available on Gendicine and to summarize important regulatory issues related to the review of the product by the SFDA. My request was met with unabashed enthusiasm and I had a draft on my desk within a month. His review, entitled "Recombinant Human Ad-p53 Treatment in China: Current Status of Gendicine," can be found on pages 1016–1027 of this issue of *Human Gene Therapy*. In this review Dr. Peng summarizes a large number of clinical trials and outlines in some detail the development and testing of the product and relevant quality control and quality assurance issues. Although the review provides a useful overview of the history of the product, it is insufficient to allow an independent assessment of the SFDA decision to approve Gendicine for commercial sales that undoubtedly involved review of thousands of pages of supporting documentation.

What have we learned from the experience of the Chinese with this gene therapy product? Clearly there is an evolving process in China to review clinical applications of gene therapy through the SFDA. For example, in 1993, 1999, and 2003, the SFDA published various *Guidance* and *Points to Consider* documents to help direct the development of gene therapy research in China (http://www.biopharm-mag.com/biopharm/article/articleDetail.jsp?id=95486). As noted in the review by Dr. Peng, the SFDA convened an expert panel of 39 scientists to review Gendicine for commercial sales, suggesting a diligent approach. On the basis of my personal experience, it would appear that Chinese scientists involved in gene therapy research are as willing to share their data as are my colleagues in the West. There is a high level of enthusiasm for gene therapy research in China, with an increasing commitment of resources being deployed for its development from both the private and public sectors. This commitment, coupled with an enormous pipeline of intellectual talent, bodes well for China to emerge as a major player in this field. The story of Gendicine also reinforces the challenges in communicating important developments in gene therapy across the globe in sufficient detail to be of practical use. I hope that you will view *Human Gene Therapy* as a venue to facilitate these kinds of communications through peer-reviewed papers, reviews, and commentaries.

James M. Wilson
Editor-in-Chief

(*See Chinese translation on next page*)

Chinese Translation of Editorial

主编专评

今又生—世界上第一个上市的基因治疗药物

最近，我刚从为期两周的亚洲之行归来。应一些亚洲同行的邀请，我访问了台湾、香港和中国大陆的一些城市。这使我能有机会与当地的一些大学及科研机构的教授和学生们就基因治疗的发展与现状进行了广泛的学术交流。在这次亚洲之行中，广州、成都及上海等城市生机勃勃的发展景象真是令人惊讶，举目望去，处处可见高耸入云的起重机群。对当地大学以及医院的访问更是给我留下了深刻的印象。我在这些大学演讲时，学生们坚持要求我用英文作报告而不用任何翻译，并积极参与对基因治疗及相关学科的深入讨论。我所访问的每一所医院都已经建立或正在建立基因治疗的临床应用转化项目，以促进对各种疾病特别是肿瘤的基因治疗方案的开展和评价。这其中有许多精益求精的项目正准备进入临床试验。

在中国令世人瞩目的基因治疗发展势头中，我一直期望能进一步了解一种名叫"今又生"的药物。"今又生"是中国深圳的生物制药企业"赛百诺基因技术有限公司"的上市产品，也是世界上第一个上市的基因治疗药物。"今又生" 以基因重组技术改造过的，非复制性的人类血清 5 型腺病毒为载体，在肿瘤细胞中表达肿瘤抑制基因 p53 从而抑制癌细胞的生长。经中国国家食品药品监督管理局（SFDA）批准，"今又生"于 2004 年 4 月上市用于治疗头颈部鳞癌（HNSCC）。根据赛百诺公司的创始人及首席执行官彭朝晖博士所提供的尚未发表的数据，截止到 2005 年 7 月 31 日，"今又生"已治疗了约 2，600 名肿瘤病人。到 2006 年预计有 50，000 名病人将会接受这种药品的治疗。同时，用"今又生"治疗其它类型肿瘤的临床试验已进入收尾阶段。

全世界基因治疗领域的同行们都在以不同的心态密切关注这一学科在中国的发展以及第一个基因治疗产品在中国的上市。无论基因治疗在哪个国家取得进展，对基因治疗的大力而广泛的支持必将有益于整个领域的进步。而且，我们大家都会得益于基因治疗产品在临床应用中的成功。但是我同时也听到一些不同的意见，包括怀疑中国药品管理监督机构对药品和治疗手段的审批制度的健全性以及中国科学家们是否愿意与世界同行们详细交流他们在"今又生"的临床评价中获取的数据。产生这种担心的其中一个重要的原因是大多数有关这一产品的临床试验结果仅仅发表在中文学术期刊上。这就妨碍了西方学者获取和分析这些重要的数据。出于这种考虑，我邀请了赛百诺公司的首席执行官彭朝晖博士为《人类基因治疗》写一篇综述来介绍"今又生"的关键性临床数据及中国 SFDA 的审批制度和过程。彭博士毫不犹豫地接受了我的邀请并在一个月之内给我送来了这篇综述。大家可以在本期 1016-1027 页读到这篇题为《用于肿瘤治疗的重组腺病毒上市基因药物"今又生"在中国临床应用的现状》的文章。

在这篇文章里，彭博士提供了大量与"今又生"相关的临床数据，介绍了这一产品的前期开发过程以及与产品的质控和质保有关的问题。这篇综述虽然概括了"今又生"的发展历程，但还不足以使我们能够独立评价 SFDA 是如何批准"今又生"上市的。要了解这一过程势必要阅读几千页的申报材料。我们在这篇文章中从中国同行那里了解到了什么呢？我们可以清楚地看到 SFDA 对基因治疗产品的临床应用的审评是一个逐渐完善的过程。例如，SFDA 在 1993，1999 和 2003 年先后三次颁布了指导原则和参照要点来帮助和指导基因治疗在中国的开展(http://www.sfda.gov.cn/cmsweb/webportal)。正如彭博士所指出，在批准"今又生"上市之前，SFDA 组织了由 39 名科学家组成的专家小组对"今又生"进行了全面的审评。这在一定程度上表明了 SFDA 对这个药物是重视和谨慎的。

在中国科学家们热衷于基因治疗的同时，中国政府和私营企业也正在增加对这一领域的投资。这种投入和中国庞大而优秀的人才队伍相结合将有效地向全世界预示：中国将在基因治疗的国际舞台上成为一个举足轻重的角色。"今又生"的故事再次强调基因治疗领域所面临的一个重大挑战，那就是如何将这一领域内的重大进展进行全球性的有效而细致的交流。我希望大家通过投交同行评审的研究文章、综述和述评的方式，把《人类基因治疗》作为这种交流的一个重要窗口。

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*本文的中文翻译由《人类基因治疗》编委，美国宾夕法尼亚大学基因治疗部高光坪博士提供。