**The Future is Now | 未来已来**

by *Jana von Hehn, PhD* | August 7, 2018

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The DNA double-helix was first postulated to be the building blocks of life by Watson and Crick in a seminal paper in 1953. Their discovery spawned a revolution in molecular biology in the 65 years that have followed, and led to the understanding of human biology, human disease and our manipulation of it. However, just several years ago, even with significant advances in the field, the idea of gene therapy to treat or cure a disorder was thought to be a distant science fiction dream. **Well, welcome to the future.**

1953 年，Watson 和 Crick 在一篇经典论文中首次提出 DNA 的双螺旋结构，并猜测它是生命的基石。他们的发现在随后的 65 年内引发了分子生物学的一场革命，并帮助了人们了解人体生物学和人类疾病，以及开发如何对抗疾病的方法。然而，尽管这个领域有很多重大进展，但就在几年前基因疗法治疗甚至治愈一种疾病的想法都还被认为是一个遥远的科学幻想。**不过，欢迎来到未来。**

Three different gene therapy products have been approved by the FDA in the last year. With gene therapies in pursuit for autoimmune diseases, heart disease, cancer, HIV/AIDs as well as genetic disorders, and continued advances with new genetic manipulation technologies such as CRISPR, the FDA is expanding how to handle gene therapy as a new and innovative approach to medicine. On July 11, 2018, Scott Gottlieb, MD, Commissioner of the FDA, announced new FDA guidances aimed at standardizing the approach companies should take as they develop and progress gene therapy programs. The FDA acknowledges that challenges exist for gene therapy that haven't existed for prior medicines and have committed to modernizing their approach to gene therapies to accommodate these new challenges.

去年，FDA 批准了三种不同的基因疗法产品。随着基因疗法对自身免疫性疾病、心脏病、癌症、HIV/艾滋病、当然还有各种遗传病的研究，以及 CRISPR 等新的基因编辑技术的不断出现，FDA 正在拓展他们的监管方法，将基因疗法作为一种新型创新式的药物来处理。2018 年 7 月 11 日，FDA 局长 Scott Gottlieb 医学博士宣布了新的 FDA 指导原则，用于规范企业在研发和推进基因治疗项目时应该采取的方法。FDA 承认，基因疗法面临着以前的药物所没有经历过的挑战，同时 FDA 也承诺对基因疗法的监管方法也会与时俱进，以适应这些新的挑战。

The FDA's main purpose is to ensure that products that reach the market are both safe and effective. Even with the 3 initial successes in treating disorders with gene therapy, there is a lot to learn, especially about the long-term impacts like durability, side-effects and potential off-target effects, which will only come with time. For gene therapy development programs long-term uncertainty is a new dilemma, but **the FDA is taking a fresh look at how to accommodate that not everything can be known in a reasonable time-frame for a market approval request without stifling development.** Robust long-term follow-up can be addressed by requiring continued development for safety and efficacy optimization with additional clinical trials after market approval. Regardless of how FDA chooses to address long-term follow-up, they remain committed to promoting safe and

effective product development through a regulatory path that maintains the gold standard in gene therapy as it has for other types of medicines.

FDA 的主要目的是确保进入市场的产品的安全性和有效性。尽管已经有 3 个治疗不同疾病的基因疗法产品取得了最初的成功，但关于基因疗法产品仍有很多东西需要研究。尤其是它的长期影响，比如持久性、副作用和潜在的脱靶效应，这些都只能靠时间来解决。对于研发基因疗法产品来说，这种远期的不确定性是一个新的困境。不过**FDA 正在重新审视当无法在一个合理的时间范围内了解到所有信息时，怎样调整监管方法来处理这类产品的上市请求，以避免将这些产品扼杀在研发阶段中。**通过要求产品在批准上市后进行进一步的临床试验，同时对产品的安全性和有效性进行持续的优化，是可以解决产品长期性问题的。不管 FDA 选择如何处理长期随访，他们仍然致力于通过一种符合基因治疗产品金标准的监管途径来保证基因治疗产品研发的安全性和有效性，就像其他类型的药物一样。

One of the new draft guidances is directed at gene therapy for rare disorders, which would apply to Rett Syndrome. More than 25 million Americans are affected by a rare disease, 80% of them are caused by single-gene disorders, half of rare diseases affect children, and almost none have effective treatments. The guidance outlines the FDA's current thinking on non-clinical studies (non-human studies) manufacturing, and clinical trial designs, and a draft version has been provided to the public for comment to ensure every angle of gene therapy development has been considered and the guidance will be thorough enough to encompass as much gene therapy development as currently possible. In the draft guidance FDA acknowledges some of the unique issues facing rare disorders such as a limited patient population, feasibility, safety, and how to measure efficacy, and the guidance is intended to assist companies in how to approach these key issues.

新的指导原则草案之一是针对罕见病的基因治疗，这也适用于 Rett 综合征。有超过 2500 万美国人受到罕见病的影响，其中 80%是由单个基因问题引起的。有一半的罕见病的患者是儿童，而且迄今为止几乎没有有效的治疗方法。指导原则概述了 FDA 当前对于非临床研究(非人体研究)所用药物的生产制造方面以及对于临床试验方案设计的思考。FDA 已发布了指导原则草案供公众讨论，以确保基因治疗技术发展过程种的每一个角度都被考虑到，同时指导原则很详细，涵盖了当前尽可能多的基因疗法发展的方方面面。在指导原则草案中，FDA 承认了罕见疾病所面临的一些独特问题，如有限的患者数量、可行性、安全性以及疗效衡量的方法，该草案的发布就是为了帮助企业解决这些关键问题。

In the face of uncertainty and the unique known and unknown challenges posed by gene therapy the FDA is not only present, but has embraced this innovative field and is committed to its success, as clearly stated by Dr. Gottlieb, "Gene therapy represents one of the most promising opportunities for developing highly effective and even curative treatments for many vexing disorders. Some of these products are almost certainly going to change the contours of medical practice, and the destiny of patients with some debilitating diseases."

在面对基因疗法带来的不确定性以及特有的已知的未知的挑战时，FDA 不仅接受，而且拥抱了这个创新领域，并致力于协助它成功。Gottlieb 博士明确表示，"基因疗法提供了一种对很多棘手的疾病的高效治疗甚至治愈的最有希望的机会。其中一些产品几乎肯定会改变现有医疗技术的边界，以及某些患有恶性疾病患者的命运。"

We are in a new era of medicine. **Are you ready?**

我们正处在医药的新时代。**你准备好了吗?**