World-Class Team Takes on Next Gen Gene Therapy

世界级团队开始迈向下一代基因疗法

by RSRT | December 13, 2018

RSRT | 2018 年 12 月 13 日

RSRT first started funding gene therapy efforts in 2010 with a collaboration between Gail Mandel, PhD and Brian Kaspar, PhD. That collaboration led to our original Gene Therapy Consortium that launched in 2014 with the inclusion of Steve Gray, PhD and Stuart Cobb,PhD.

2010 年，RSRT 与 Gail Mandel 博士和 Brian Kaspar 博士合作，第一次开始资助基因疗法的研究。这项合作逐渐成为演进为我们最初的基因治疗联盟。在 Steve Gray 博士和 Stuart Cobb 博士加入后，该联盟于 2014 年正式成立。

The Consortium worked through numerous challenges involving vector optimization (the Trojan horse that delivers the gene into a cell), gene construct optimization (what you package into the vector that regulates MeCP2 protein production), gene therapy dosage, and the best route to deliver it.

联盟开展了非常多的有挑战性的工作，包括优化载体（载体就好比将基因输送进细胞内的特洛伊木马）、优化基因结构（即载体里承载的用于调节 MeCP2 蛋白质生成量的元件）、以及研究基因疗法的剂量和输送基因疗法的最佳途径。

The data generated by the Consortium exceeded our expectations. They were able to develop a gene therapy product candidate with impressive efficacy, safety and delivery characteristics. Importantly, the magnitude of improvement in the mouse models of Rett is much greater than that of any drug tested to date and suggests that significant benefit may be achieved in people. Based on that data AveXis committed to advancing a gene therapy candidate into clinical trials, and is on track to launch the first trial early in 2019.

联盟工作的成果超出了我们的预期。他们已能开发出一种有希望的候选基因疗法产品，其在治疗效果、安全性和易输送性等方面都有引人瞩目的表现。最重要的是，这种产品在 Rett 小鼠模型上达到的病情改善幅度远远大于迄今为止所测试的其它任何药物。这也表明这种产品在人身上可能也会取得显著的效果。基于这些数据，AveXis 公司已经在推动把一种候选基因疗法进入到临床试验阶段，并将按计划在 2019 年初启动首次试验。

While we fervently hope that the AveXis trial delivers significant and dramatic results we suspect there will be room for improvement. Fortunately, technological advances in gene therapy are happening quickly with more effective vectors being discovered that can carry larger DNA cargos and target a greater percentage of brain cells.

虽然我们热切希望 AveXis 的临床试验能取得显著结果，但我们认为对于基因疗法而言仍有改进的空间。幸运的是，基因疗法的技术正在飞速发展，更有效的载体在不断被发现。这些载体可以携带更多的 DNA，并能影响到更多比例的大脑细胞。

So today we announce a Gene Therapy Consortium 2.0 comprised of a world-class team: James Wilson, Adrian Bird and Stuart Cobb. The goal will be to have a next generation gene therapy product…should we need it.. ready for clinical testing by 2021.
因此，今天我们在这里宣布基因治疗联盟 2.0 成立，这是一个世界级团队，成员包括 James Wilson，Adrian Bird 和 Stuart Cobb。2.0 版联盟的目标是研发生产下一代基因治疗产品（如果我们需要的话）。准备在 2021 年前进行临床试验。

James Wilson, MD, PhD, is a pioneer and a leader in the gene therapy field for decades and has played a pivotal role in the renaissance that the field is currently experiencing. He made a number of seminal discoveries including the discovery and development of the adeno-associated virus (AAV) that will be used by AveXis in the upcoming clinical trial. One of Dr. Wilson's overarching objectives is improving delivery of genes to the brain which is of course extremely relevant to Rett Syndrome. Dr. Wilson is at UPENN where he runs the largest worldwide academic gene therapy program.
James Wilson，医学博士，他在近数十年来一直是基因治疗领域的先驱和领导者，在基因治疗概念的最近一轮复兴中发挥了关键作用。他做出了许多开创性的发现，包括发现和开发腺相关病毒（AAV），这种病毒就是 AveXis 将在临床试验中使用的病毒载体。Wilson 博士的首要研究目标之一是改进基因向大脑的输送的方式，这显然与 Rett 综合症的需求密切相关。Wilson 博士同时也在宾夕法尼亚大学管理着世界上最大的学术型基因治疗项目。

We welcome Adrian Bird, PhD of the University of Edinburgh to the Gene Therapy Consortium. As the world's leading expert on MECP2 Professor Bird has become synonymous with Rett research. He discovered the MeCP2 protein in the early 1990s; made a mouse model that is used in hundreds of labs around the world; published the landmark paper that established the principle of reversibility for the disorder; and has made many significant contributions to the understanding of the function of the MeCP2 protein. Adrian Bird is a founding trustee of RSRT.
我们同时欢迎爱丁堡大学的 Adrian Bird 博士加入基因治疗联盟。作为世界领先的 MECP2 专家，Bird 教授已经成为 Rett 综合症研究的同义词。是他在 20 世纪 90 年代初发现了 MeCP2 蛋白，是他开发出了现已在世界各地的数百个实验室中使用的研究用小鼠模型，还是他发表了那篇关于 Rett 疾病机能失调的可逆性原则的里程碑式的论文。除此之外，他还为人类了解 MeCP2 蛋白的功能做出了许多重要贡献。Adrian Bird 也是 RSRT 的创始董事。

Rounding out the Consortium is an original member, Stuart Cobb, PhD. He recently moved from the University of Glasgow to the University of Edinburgh where he and his lab members work closely with Professor Bird. Dr. Cobb's introduction to Rett came well over 10 years ago when he was approached by Professor Bird to conduct some neurophysiology experiments. He was a co-author on the 2007 reversibility paper and published the first gene therapy study in male mice using AAV2 and AAV9 vectors. Besides traditional gene therapy strategies Dr. Cobb is also pursuing RNA modification approaches.

原有的成员 Stuart Cobb 博士也加入了这个联盟。他最近从格拉斯哥大学搬到了爱丁堡大学，在那里他和他的实验室成员与 Bird 教授密切合作。十多年前，Bird 教授就曾邀请 Cobb 博士做一些神经生理学实验。这是 Cobb 博士进入 Rett 研究界的开端。他是 2007 年 Rett 疾病可逆性论文的合著者，发表了第一个使用 AAV2 和 AAV9 载体对雄性小鼠进行基因治疗的研究。除了传统的基因治疗策略，Cobb 博士还在研究 RNA 修饰方法。

Gail Mandel continues to be a core member of our team and is funded through the MECP2 Consortium. She will remain an advisor to the Gene Therapy Consortium.
Gail Mandel 仍然是我们团队的核心成员，她的研究由 MECP2 联盟资助。她将继续担任基因治疗联盟的顾问。

The Gene Therapy Consortium 2.0 has almost $2.5 million in funding from RSRT.
基因治疗联盟 2.0 已从 RSRT 获得了近 250 万美元的研究经费。

The goals of the Consortium include:

- More deeply understand the function of MECP2 to develop more effective gene therapy products
- Design novel gene therapy cassettes to enable better regulatory control of the MeCP2 protein
- Design tunable systems that allow gene therapy to be turned off if necessary

联盟的目标包括:

- 更深入了解 MECP2 基因的功能，从而研发更有效的基因治疗产品
- 设计新的能更好调控 MeCP2 蛋白质表达量的基因治疗元件
- 设计可调整的系统，以便在必要时关闭基因治疗的功能

This exciting work is made possible by all RSRT's generous supporters and through the passion and commitment of Rett families in the US and abroad who fundraise for us. Thank you to each and every one of these families for taking action and best wishes for speedy progress to the Consortium.
感谢所有 RSRT 慷慨的支持者和协助 RSRT 筹款的美国和世界各地的 Rett 家庭，他们的热情和努力让这项激动人心的工作得以实现。感谢每一个采取了行动的家庭，让我们共同祝愿该联盟能迅速取得进展。