On the Shoulders of Giants

站在巨人的肩上

by Randy Carpenter, Jana von Hehn and Tim Riley | January 24, 2019

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2019 started with the exciting announcement that our 2018 research awards totaled $10 million! We take our hats off to the hundreds of Rett families who put their urgency and passion to work raising funds and to our colleague, Tim Freeman, who leads this impressive effort. Although we personally are typically not involved with RSRT's fundraising activities we can imagine how difficult it is to raise the dollars necessary to support our Roadmap to a Cure. It is our responsibility to wisely invest your fund raising dollars – and it is a responsibility we take very seriously.

在 2019 年来临时，我们非常激动地宣布，在 2018 年我们总计资助了 1000 万美元的研究资金！我们向成千上万个 Rett 家庭致敬，他们带着使命感和热情投入到筹款工作中。我们也向我们的同事 Tim Freeman 致敬，是他领导了这项令人印象深刻的工作。尽管我们通常不直接参与 RSRT 的筹款活动，但我们可以想象筹集支持我们 Roadmap to a Cure（治愈路线图）项目所需的资金是多么困难。现在，将你们募集到的资金做明智地投资是我们的责任——我们将非常认真对待的责任。

Be Vigilant for Breakthrough Discoveries! This is a vital ideal that we all share and try to live up to every day. When we identify a discovery that can be applied to Rett Syndrome, we actively recruit the pioneering researchers to our cause – with a primary emphasis on therapeutics that could be curative. Recruiting leading scientists' focus and energy to Rett isn't always easy, as other disorders with less hurdles to jump are often more attractive. So it's fortunate that we are a tenacious bunch. The proposals funded this year are a direct product of this proactive and sometimes relentless strategy.

对各种突破性发现保持警觉！这是一个我们大家共同拥有，并每一天为之努力的最高理想。当我们鉴别到一项有可能用于雷特综合征的科学发现时，我们会积极招募那些前沿研究人员参与我们的事业——对那些有可能治愈疾病的疗法我们会重点关注。将顶尖科学家的注意力和精力吸引到雷特综合征上并不总是件容易的事，因为其他治愈障碍较少的疾病往往对研究人员更有吸引力。幸运的是，我们是一群顽强的人。今年我们资助的研究计划就是这种积极主动、不言放弃的战略的直接产物。

We have been carefully monitoring progress with CRISPR, meeting with the leading scientists and encouraging them to apply CRISPR to Rett. Fortunately, CRISPR technology has now expanded to allow CRISPR to function like an eraser rather than a scissor, an important development that opens the door for difficult-to-treat neurological disorders. The awards to Beam Therapeutics and MIT leverage these recent scientific discoveries and aim to correct mutations that cause Rett Syndrome in brain cells at the level of both DNA and RNA.

我们一直在密切关注 CRISPR 的进展，我们已经与学术界顶尖科学家会面并鼓励他们将 CRISPR 应用于 Rett。幸

运的是，CRISPR 技术现在已经扩展到允许 CRISPR 像橡皮而不是剪刀一样工作，这是一项重要的发展，为各种难以治疗的神经系统疾病打开了大门。我们向 Beam 药业公司和麻省理工学院提供资助，目标是利用这些最近的科学发现来探究同时在 DNA 和 RNA 水平上纠正那些导致雷特综合征的脑细胞基因突变的方法。

The two awards to UMass Medical School, take advantage of top talent in their RNA Therapeutics Institute, where Nobel Prize winners and CRISPR company founders expand scientific knowledge every day. One program aims to replace the entire section of MECP2 DNA where most mutations occur with a normal section that is mutation free. This approach would allow 97% of our Rett patients to be treated with just one gene editing approach! The other UMass program aims to trick MECP2 mutant cells into ignoring their mutation and making functional protein. Although this particular approach would benefit only those patients with certain mutations (those that end in X), about 1/3 of the Rett patient population could be helped. This program will use a treatment that the FDA is already familiar with, which would speed development if it proves to work in Rett.

我们给予马萨诸塞州立大学医学院(UMass Medical School)两项资助，利用该校 RNA 疗法研究所(RNA Therapeutics Institute)——诺贝尔奖得主们和 CRISPR 公司创始人们每天都在探讨拓展科学知识的地方——的顶尖人才的优势开展研究。一个项目的目标是将 DNA 中大多数突变发生的 MECP2 基因的全部片段替换为一个正常无突变的片段。这种方法可以让 97%的 Rett 患者用一种基因编辑方法进行治疗！另一个在马萨诸塞州立大学医学院进行的项目的目标是诱导有 MECP2 突变的细胞忽略它们的突变，并产生有功能的蛋白质。虽然这种特殊的方法只对那些具有特定突变的患者(那些突变以 X 结尾，导致蛋白质翻译提前终止的患者)有效，但是也能帮助到约 1/3 的 Rett 患者。这个项目将使用 FDA 已经熟悉的一种治疗方法，这会加速它的研发进度——如果这种疗法能证明对 Rett 有效的话。

Importantly, all of these approaches will only correct cells that make mutant MECP2, which reduces the risk of making too much MECP2, thereby providing a potential advantage over current gene therapy approaches.

重要的是，所有这些方法都仅仅会纠正产生 MECP2 基因突变的细胞，从而降低产生过多 MECP2 蛋白的风险，因此相对于目前的基因疗法具有一定的潜在优势。

Our primary goal in funding cutting-edge research programs like these is to advance them to a stage where biopharma companies can take them forward. The success of our Gene Therapy Consortium 1.0 in partnering with AveXis/Novartis is proof that this is possible – a strategy we seek to repeat with all of our curative approaches. Our ultimate goal is to deliver life-altering therapeutics as soon as possible. We won't rest until we have achieved that.

我们资助这类最前沿研究项目的主要目标是推动这些技术的发展，直到它们能被生物制药公司所应用的地步，然后生物制药公司将进一步推动技术产品化。我们的基因治疗联盟 1.0 与 AveXis/Novartis 合作的成功证明了这种方式的可行性——我们将在寻求其它所有治疗方法中继续应用这一策略。我们的最终目标是尽快将那些改变生活的疗法带给病人。在达到这一点之前，我们绝不停歇。