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Rett Syndrome Research Trust Awards $10 Million to Preeminent Researchers in Pursuit of Curing Devastating Neurological Disorder

雷特综合征研究信托基金向治愈破性神经疾病的杰研究者们提供1,000万美的资助

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TRUMBULL, CT — Thanks to a $10 million investment in Rett Syndrome research in 2018—the largest annual award since the organization was founded in 2008 - the Rett Syndrome Research Trust (RSRT) is fueling exciting new collaborations and advances from an international group of world-class scientists that offer new hope for families coping with this devastating disease. Total research awards to date by RSRT have reached $57 million.
美国康涅狄格州 TRUMBULL 消息，得益于雷特综合征研究信托基金（Rett Syndrome Research Trust，RSRT）在 2018 年资助的 1000 万美元在雷特综合征上的研究——这是该组织自 2008 年成立以来资助金额最大的一年——各种令人兴奋的新行合作得以促成，一个世界级的科学家组成的国际组织也被推动建立，这些都为所有面对这种破坏性疾病的家庭带来了新的希望。迄今为止，由 RSRT 资助的各项研究经费总额已达到 5700 万美元。

Rett Syndrome is caused by mutations in a gene known as *MECP2* resulting in a constellation of serious, progressive and disabling neurological symptoms that emerge during early childhood and eventually rob sufferers of the ability to speak, move normally or use their hands, among other devastating deficits.
雷特综合征（Rett Symdrome，RTT）是由一种名为 MECP2 的基因突变引起的疾病。基因突变会导致在儿童发育早期开始出现一系列严重的、发展性的、使人丧失能力的神经系统症状，最终会使患者丧失语言、正常行动或使用双手的能力，以及其他一些毁灭性的缺陷。

Yet there is reason for optimism, now more than ever. Early in 2018, RSRT made a decision to increase investment in several key areas and to recruit elite scientists to execute in these areas. These areas include 1) gene therapy, where healthy copies of the *MECP2* gene are introduced to compensate for mutated ones 2) DNA editing, where a specific mutation in the genome is targeted and permanently corrected and 3) RNA editing, which focuses on correcting mutations in RNA. Given that DNA and RNA editing can be achieved in a number of different ways, RSRT is simultaneously pursuing all possible modalities to be sure to cover every therapeutic avenue.
不过现在比过去任何时候都更有理由乐观。2018 年初，RSRT 决定增加对几个关键领域的投资，招募优秀科学家在这些领域开展工作。这些领域包括:1)基因疗法，即引入健康的 MECP2 基因拷贝来补偿突变的 MECP2 基因；2)DNA 编辑，即靶向基因组中的特定突变将其并永久修改纠正；3)RNA 编辑，即专注在 RNA 层面上纠正突变。鉴于 DNA 和 RNA 编辑都可以通过多种不同的方式实现，RSRT 正在同时研究所有可能的模式，以确保覆盖所有治疗途径。

The new awards are being made as part of RSRT's four-pronged strategic research plan—the *Roadmap to a Cure*—including the components *Cure, Treat, Enable,* and *Learn.*
这些新增的投资也是 RSRT 四管齐下的战略研究计划 the Roadmap to a Cure（包括治愈、治疗、使能、学习四个方面）的一部分。

"At RSRT we have one bold, challenging goal – to cure Rett and related *MECP2* disorders. To that end, RSRT has developed the first and only comprehensive and aggressive plan to cure Rett Syndrome. The strategies are identified, the scientists recruited and our internal research team poised to not only monitor and evaluate progress but to also be vigilant for new technologies on the horizon," said Monica Coenraads, RSRT's Executive Director. "Our important work is made possible by the passion and urgency of families affected by Rett who fundraise for us. As a parent of a young woman with Rett I am beyond grateful for these efforts. Our success will require the continued support of these families and beyond."
RSRT 的执行董事 Monica Coenraads 表示："在 RSRT，我们有一个大胆的、有挑战性的目标——治愈 Rett 和相关的 MECP2 疾病。为此，RSRT 制定了第一个也是唯一一个全面的积极计划来治愈雷特综合征。我们的战略已经确定，招募的科学家和我们内部的研究团队不仅在持续观察和评估研究进展，而且时刻对新出现的新技术保持敏感。"她还说："是那些所有协助我们筹款的受雷特综合征影响的家庭，他们的热情和紧迫感让我们这些重要工作得以开展。作为一个和患有雷特综合征的年轻女孩的母亲，我对这些努力感激不尽。我们的成功需要这些家庭以及更多家庭的持续支持。"

The following are highlights of the projects that earned an RSRT award in 2018, all of which focus on the vital first component of the *Roadmap*—a cure:
以下是 2018 年 RSRT 资助的各个项目的重点介绍，所有这些项目都聚焦于在战略研究计划（Roadmap）的第一个重要组成部分——治愈：

- Almost **$700,000 in additional funding for the *Gene Therapy Consortium 2.0.*** In 2014 RSRT conceived of and launched the *Gene Therapy Consortium 1.0*. Data generated by this *Consortium* led to the company AveXis' decision to pursue gene therapy trials in Rett Syndrome individuals, set to begin this year. In the meantime, RSRT has recruited James Wilson, MD, PhD, to *Consortium 2.0*, leader of the world's largest academic gene therapy program at the University of Pennsylvania. He joins Adrian Bird, PhD and Stuart Cobb, PhD both from the University of Edinburgh. The goal of *Consortium 2.0* is to get a next generation gene therapy product ready for clinical testing by 2021.
  基因治疗联盟 2.0 项目，获资助近 70 万美元。在 2014 年，RSRT 筹备并启动了基因治疗联盟 1.0 项目。这个联盟研究得到的数据促使 AveXis 公司决定今年初开展在雷特综合征患者个体中进行基因治疗的临床试验。与此同时，RSRT 聘请了医学博士 James Wilson 加入联盟 2.0，他是宾夕法尼亚大学(University of Pennsylvania)全球最大的学术性基因治疗项目的负责人。他加入了爱丁堡大学（University of Edinburgh）的 Adrian Bird 博士和 Stuart Cobb 博士的行列。联盟 2.0 的目标是研究下一代记忆治疗产品，并目标在 2021 年开展临床试验。

- **Nearly $2 million to Beam Therapeutics for a DNA editing program to correct *MECP2* mutations.** Founded by Keith Joung, PhD, designated as one of the most cited researchers worldwide; David Liu, PhD, named by *Nature* as one of 2017's top 10 researchers in the world; and Feng Zhang, PhD, one of the pioneers of the CRISPR gene editing field, Beam is applying the cutting-edge gene editing tool known as CRISPR to target specific point mutations in DNA and permanently fix them. This exciting project harnesses the expertise, resources, and industrial approach of Beam to discover a novel class of therapeutics for Rett Syndrome.
  Beam Therapeutics 公司，获资助约 200 万美元用于纠正 MECP2 变异的 DNA 编辑项目。Beam Therapeutics 由三位科学家创建，他们是：Keith Joung 博士，他被公认为世界上被引用最多的研究者之一；David Liu 博士，他被 Nature 杂志评选为 2017 年全球十大研究者之一；还有张锋博士，他是研究 CRISPR 进行基因编辑领域的先驱之一。Beam 正在研究这种最前沿的 CRISPR 技术，将其作为基因编辑工具来针对 DNA 中特定

突变点位进行编辑从而一劳永逸的修复基因。这项令人兴奋的项目会利用 Beam 的专业知识、资源和产业化方法，来研究针对雷特综合征的新一类治疗方法。

- **More than $2.3 million to correct *MECP2* mutations in RNA.** Led by investigators Guoping Feng, PhD, Feng Zhang, PhD, and Robert Desimone, PhD of MIT, the Broad Institute and Harvard University, this project will develop therapeutics using Zhang's CRISPR Cas13 technology to target RNA rather than DNA.
  在 RNA 层面纠正 MECP2 突变项目，获资助逾 230 万美元。该项目由麻省理工学院、Broad 研究所和哈佛大学的几位科学家冯国平博士、张锋博士和 Robert Desimone 博士主导，将利用张锋的 CRISPR Cas13 技术开发靶向 RNA 而非 DNA 的疗法。

- **More than $2.4 million for RNA and DNA editing to treat Rett Syndrome.** Jonathan Watts, PhD and his colleagues will put their deep knowledge of RNA chemistry to work developing RNA editing therapeutics. Their institution, University of Massachusetts Medical School, is renowned for their work on RNA with faculty receiving both a Nobel and a Breakthrough Prize. For DNA editing the aim will be to replace the two exons where 97% of *MECP2* mutations reside.
  用于治疗雷特综合征的 RNA 和 DNA 编辑项目，获资助逾 240 万美元。Jonathan Watts 博士和他的同事们将把他们对 RNA 化学的深刻了解用于开发 RNA 编辑疗法。他们所在的麻省大学医学院(University of Massachusetts Medical School)因其在 RNA 方面的研究而闻名，学院的科学家曾获得过诺贝尔奖和突破奖(Breakthrough Prize)。DNA 编辑的目标是替换掉基因的 2 个外显子，有 97%的 MECP2 突变都位于这 2 个区域。

- **Almost $1 million to two RNA editing projects** being undertaken in the lab of long-time Rett researcher Gail Mandel, PhD and her colleague, John Sinnamon, PhD of Oregon Health and Sciences University and newcomer to Rett, Peter Beal, PhD of University of California Davis. These two West Coast labs are editing RNA by leveraging the naturally-occurring editing enzyme in neurons known as ADAR.
  两个 RNA 编辑项目，获资助约 100 万美元。项目目前还处于实验室研究阶段，由长期致力于 Rett 研究的 Gail Mandel 博士和她的同事，Oregon Health and Sciences University 的 John Sinnamon 博士，以及新加入的 University of California Davis 的 Peter Beal 博士承担。这两个西海岸的实验室正在采用 ADAR（一种神经元中自然产生的编辑酶）来编辑 RNA。

List of 2018 Awards
2018 年资助清单（译略）

Adrian Bird/Stuart Cobb
University of Edinburgh
Gene Therapy Consortium 2.0
$653,856

BEAM Therapeutics
Developing a pre-clinical DNA base editing program to precisely correct the genetic cause of Rett Syndrome in the central nervous system
$1,870,660

Jonathan Watts/Scot Wolfe/Eric Sontheimer/Anastasia Khvorova
University of Massachusetts

RNA and Genome editing for treatment of Rett Syndrome
$2,403,735

Guoping Feng/Feng Zhang/Robert Desimone
Massachusetts Institute of Technology/Broad Institute/Harvard University
RNA-editing as a gene therapy approach for Rett Syndrome
$2,332,000

John Sinnamon
Oregon Health and Sciences University
New editing enzymes for RNA
$345,000

Peter Beal
University of California Davis
New molecular tools for directed editing of MECP2 mutations associated with Rett Syndrome
$563,870

Allan Jacobson/Jonathan Watts
University of Massachusetts Medical School
Read-through of premature termination codons for treatment of Rett Syndrome
$323,000

Andrea Cerase
Queen Mary University of London
Reactivation of MECP2 and CDKL5 genes by functional deactivaton of Xist RNA
$351,022

Additional Funding/Bridge Funding

David Lieberman
Boston Children's Hospital
Clinical Trial Consortium
$74,792

Victor Faundez
Emory University
Outcome Measures and Biomarkers Development
$40,480

Antonio Bedalov
Fred Hutchinson Cancer Research Institute
Reactivating MECP2
$38,000

Autism Science Foundation
$17,500

MECP2 Duplication Syndrome

Huda Zoghbi

Baylor College of Medicine
A forward genetic screen to identify druggable modulators of MECP2 levels
$752,660

About the Rett Syndrome Research Trust

The Rett Syndrome Research Trust (RSRT) is a nonprofit organization with a highly personal and urgent mission: a cure for Rett Syndrome and related MECP2 disorders. RSRT operates at the nexus of global scientific activity enabling advances in knowledge and driving innovative research. In March of 2017 RSRT announced Roadmap to a Cure, a three-year, $33 million strategic research plan. The plan, for which $24 million has been pledged or contributed by generous donors, prioritizes four curative approaches with gene therapy as our lead program. In June of 2017 the biotechnology company, AveXis, announced its intent to advance RSRT's gene therapy program to clinical trials. Since 2008, RSRT has awarded $57 million to research. To learn more, please visit www.reverserett.org

关于雷特综合征研究信托基金会

雷特综合征研究信托基金会(Rett Syndrome Research Trust，RSRT)是一个非营利组织，其有一个高度个体化和紧迫性的目标：治愈雷特综合征和相关的 MECP2 疾病。RSRT 以全球科学活动为纽带，促进知识进步，推动创新研究。在 2017 年 3 月，RSRT 宣布了一项为期三年、耗资 3300 万美元的战略研究计划——Roadmap to a Cure。目前该计划已经得了各位慷慨的捐赠者贡献的 2400 万美元。计划中将四种以基因疗法为主导的治疗方法列为优先项目。在 2017 年 6 月，生物技术公司 AveXis 宣布将 RSRT 的基因治疗项目推向临床试验。自 2008 年以来，RSRT 已向各种研究资助 5700 万美元。想了解更多信息，请访问 www.reverserett.org。

About Rett Syndrome

Rett Syndrome is a genetic childhood neurological disorder caused by random mutations of the MECP2 gene on the X chromosome that affects predominately girls but can rarely also affect boys. Its symptoms typically become apparent between the ages of 12 to 18 months. Rett Syndrome is devastating as it deprives young children of speech, hand use, and normal movement often including the ability to walk. As the children enter childhood the disorder brings anxiety, seizures, tremors, breathing difficulties, and severe gastrointestinal issues. While their bodies suffer, it is believed that their cognitive abilities remain largely intact. Although most children survive to adulthood, they require total round-the-clock care.

关于雷特综合征

雷特综合征（Rett Syndrome，RTT）是由 X 染色体上 MECP2 基因的随机突变引起的一种遗传性儿童神经系统疾病，主要影响女孩，但也有罕见的男孩受影响。其症状通常在 12 至 18 个月之间逐渐出现。雷特综合征是一种毁灭性的疾病，它剥夺了幼儿的语言能力、使用手的能力和正常的运动（通常也包括行走）能力。当孩子进入到儿童时期，这种疾病会带来焦虑、癫痫、震颤、呼吸困难和严重的肠胃问题。虽然他们的身体受到各种伤害，但通常认为他们的认知能力基本保持完好。尽管大多数孩子能生存到成年后，但他们需要全天 24 小时的照料。