

Moving the Needle

攀登新高峰

by *Timothy Riley, PhD* | October 29, 2018

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I have always enjoyed the creative process. In my younger days, I was fond of cooking, which was not always sanctioned as an appropriate activity for a young boy in that era of our society. As I moved forward with my high school education, I had an intense interest in science. In fact, when an AP chemistry class was going to be denied us due to lack of enrollment, the dozen or so of us who did sign up for the class marched into the principal's office and demanded that the class be offered. I am sure you can imagine the ruckus that caused. However, we succeeded in getting the class. I have made a career of swimming upstream and proving dogma wrong, even at the risk of my job at times. Some might even say tilting with windmills. I think that spark of fighting against the odds is what provides a link between the Rett family community and me. I can relate in a small way to Rett families due to the devastating chronic challenges of mental illness in my own family, both birth and adopted members. These are however infinitesimally small challenges compared to what Rett individuals and their families face on a daily basis. I am totally sincere when I say with great admiration that what Monica Coenraads and the whole RSRT team has accomplished in ten years is nothing short of miraculous. The stage is now set to make extraordinary advances.

我一直很享受创造的过程。我在小时候很喜欢烹饪，虽然这是一种在我们那个时代社会上多少认为对小男孩来说不太合适的活动。当我长大一些升入高中后，我开始对科学产生了浓厚的兴趣。举个例子，当时跳级化学课（Advanced Placement Chemistry，美国高中选修的一门涵盖大学化学知识的课程）因为报名人数不足而拒绝开班时，我和十几个其它报名的学生一起闯进校长办公室，要求开设这门课。我保证你能想象当时引起的骚动。不过，我们最终还是成功地上了这门课。我的职业生涯总是逆主流而行，甚至有时冒着丢掉工作的风险去证明某些公认法则是错误的。有些人评价这就堂吉诃德斗风车一样危险。我想，这种勇于克服困难的闪光点就是将我和 Rett 家庭社区联系起来的纽带吧。由于我自己的多位家庭成员（包括亲生的和领养的）都面临着严重的慢性精神疾病的困扰，所以我和 Rett 家庭是有一些相似点的。不过，同 Rett 个体及其家庭每天所面临的诸多挑战相比，我所面临的挑战可以说是微不足道。我由衷地钦佩 Monica Coenraads 和整个 RSRT 团队，他们在十来年间取得的成就只能用奇迹来形容。现在他们又将在新的一个阶段开始取得非凡的新进展。

There is an alignment of planets right now for new technologies that need the expertise of folks such as Randy Carpenter, Jana Von Hehn and myself to translate them to actual products that can move to the clinic in a few years. I am excited about the early trials in gene therapy with the AveXis/Novartis team. My decades in drug development, however, have taught me that it is an iterative process. Rarely does the first round of a new technology work to the level that will satisfy the entire Rett community. I am therefore committed to moving as many interventions to the clinic as make technical and medical sense. I personally would like to see 4 to 5 interventions move to the clinic in the next 3 to 5 years. They include a second-generation gene therapy, DNA editing, RNA editing, protein augmentation, and possibly a read through or MECP2-reactivation approach.

对那些需要由 Randy Carpenter, Jana Von Hehn 和我这些具有专业知识的人来转化成在几年内能应用于临床的实际产品的新技术来说，现在正是一个千载难逢的好机会。我对 AveXis/Novartis 团队的基因疗法的前期试验感到兴奋。不过，我在药物研发上的几十年的经验告诉我，这会是一个反复的过程。新技术的第一阶段的结果恐怕很难达到让整个 Rett 社区都满意的水平。因此，我决心将尽可能多的治疗措施推向临床。我个人希望在未来的 3 到 5 年内，能有 4 到 5 个治疗措施进入到临床阶段。它们包括第二代基因疗法、DNA 编辑、RNA 编辑、蛋白质增强，可能还包括基因通读或 MECP2 再激活方法。

This vision is extraordinarily aggressive, but that is the only way I see that drug development should and can move forward. I have moved the needle before in my drug development career. My team worked with our major pharma partner to move Adynovate from concept inception all the way to the market. We also developed an opioid that does not cause addiction from invention to successful phase 3 and now an NDA submitted to the FDA. I want to move that needle again in a big way with Rett Syndrome.

这个远景看上去非常激进，但这是我认为药物研发应该而且能够向前发展的唯一途径。在我的药物研发职业生涯中，我曾经攀登很多高峰。我的团队与我们主要的药品合作商一起将 Adynovate（一种针对血友病的药物）从概念形成开始一直推进到市场。我们还研发出一种非成瘾性片阿片类药物，从发明出来到现在已经成功完成三期临床试验，现在也向 FDA 提交了 NDA (New Drug Application) 申请。现在，我想在雷特综合征领域来一个大动作，攀登上一个新的高峰。

I hope to meet as many of you as possible in the months to come. In the meantime if you have any questions I can help with don't hesitate to contact me. timriley@rsrt.org

我希望在今后的几个月里能尽量多的与你们见面。在此期间，如果你们有任何我可以帮助的问题，请不要犹豫，马上与我联系：timriley@rsrt.org