科研学术之路的10条经验

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引言：Ronald D Vale教授 1959 年出生在美国加州好莱坞。21 岁毕业于加州大学圣塔芭芭拉分校，专业生物和化学。之后在斯坦福大学念双博士(哲学博士-医学博士)，在26岁获神经生物学哲学博士。因为他的研究生记录太好，他就只要哲学博士，不要医学博士。27岁成为助理教授，35 岁做正教授，42岁当选美国科学院院士。美国艺术与科学学院院士以及美国国家科学院院士双料院士。自 1995年以来，一直担任霍华德·休斯医学研究所研究员。也是诺贝尔奖热门人选。1985年，在Sheetz和Reese实验室，年仅26 岁的Ron Vale，一年内发表了 5 篇 Cell，其中 4篇是第一作者，记录保持至今，未被打破。2012年，他和迈克尔·希茨和詹姆斯·斯普迪赫共同获拉斯克基础医学研究奖。获奖后，更是把他的获奖感言：自己的求学经历和总结的十条科研经验(top-ten list)发表在了Nature Medicine 杂志上，题为：How lucky can one be? A perspective from a young scientist at the right place at the right time，以下为文中 Ten lessons中文译文及英文原文，分享给大家。

01.找到好导师，学习他们然后发展出自己的风格。

Find good mentors, learn from them and then develop your own style.

三人行，必有我师。科学既是一个实验过程，也是一个处理问题的哲学、个人研究风格和与他人合作本身就是一个实验的过程。作为一名年轻的科学家，你要接触不同的科研方法，从资深的前辈科学家那里汲取思想和治学态度，加以消化吸收，最终沉淀出最适合自己的一种风格，这会让你具有你所钦佩的人的气质特征。对他人不卑不亢，既不盲目崇拜也不轻蔑轻视。我很幸运，遇到了很多伟大的导师，其中包括Bruce Schnapp, Tom Reese, Mike Sheetz和Jim Spudich的核心团体。他们每个人都有独特的个性和科研方法，这让我受益匪浅。但他们有一个共同点：都非常友善，把我当做一个年轻的科学家来支持。我研究生时还遇到其他的贵人：首先是我的导师Eric Shooter。想想，有几位论文导师能由着他的研究生游离在导师的课题之外，做一些与实验室工作无关的事?而且任由其对学分一点都不上心?那个时候，我还没有完全意识到，和其他许多科学家相比，Eric对他的实验室“家庭”是多么的无私。在MBL，我还遇到了Shinya Inoue和Andrew Szent-Gyorgyi等活跃的老科学家。他们在Woods Hole的冬季收留了我这个从西海岸来的孩子，他们的实验室小而专一(不同于斯坦福的大型实验室)，他们热爱生活，热爱科研，实现生活和科研的完美统一，不偏废其一。

Soak up your surroundings. Science is as much about philosophies of approaching problems, personal styles

of research and working with others as the process of experimentation itself. As a young scientist, you need to be exposed to different ways of doing science, absorbing the ideas and attitudes of more senior scientists.The net result is a maturation of a hybrid style that best suits you and is a composite of the characteristics that you admire in different individuals. Neither idolize nor ignore anyone. I was fortunate to have many great mentors, which included the core group of Bruce Schnapp, Tom Reese, Mike Sheetz and Jim Spudich. I gained tremendously from their unique personalities and scientific approaches. But they all shared one thing in common—they were incredibly kind and supportive of me as a young scientist. I had additional heroes in graduate school. First was my wonderful advisor, Eric Shooter. How many thesis advisors would let their graduate student wander off quite a distance to work on a project unrelatedto his or her own lab ’ s work and without anythought of gaining credit for something that might emerge? I did not completely appreci-ate at the time how different Eric' s unselfishattitude about his lab ' family' is from that ofmany scientists. I also met lively older scien-tists at the MBL-Shinya Inoue and Andrew Szent-Gyorgyi who ' adopted' this kid from the West Coast during the Woods Hole winter.They had small and focused labs (unlike the generally larger labs at Stanford) and merged alove of life and a love of science without com-promising either.

02. 选择一个重要的问题。

Pick an important problem.

每个人都一样，都喜欢去解决有趣的，令人着迷的问题，而不喜欢沉闷无聊的问题。但是，确定一个既重要又亟需解决的选题并非易事。况且，我们还必须在规定的时间节点内完成对应的结果，才能获得学位、工作或者资助。这使得我们中的大部分人在大多数时间里，精力并不是专注于生物学中的大问题上。但是，如果你想不一样，在一些重要问题上，你必须实时跟进，时刻保持警惕，比别人多思考一点，哪怕超出了你的研究范围或你的专长，从而找到一个重大问题的突破口。如果机会来了(见下一建议)，千万别错过，抓住它。在大多数情况下，如果你一时候没能提出一个重要的问题，你基本不可能做出重大成果。

Everyone would rather solve a fascinating problem than a boring one. However, it is not easy to identify a project that is both important and ripe forsolving. Furthermore, pragmatics dictate get-ting results in a defined time period in order to obtain a degree, job or grant. As a result, most of us are not always working on grand issues in biology all of the time, However, you should be vigilant and thoughtful, loking for a wedge or an opening to tackle an important problem, even if it is not in your area of research or expertise. If the opportunity comes along (see next point), seize it.In most cases, you cannot make an important discovery if you are not asking an important question from the start.

03. 奋力领先，勇于冒险，敢于放手一搏。

Get ahead but then take a chance: seek adventure.

在Eric Shooter实验室的头两三年里，我发表了几篇很扎实但并不出色的论文，但我知道，这些论文已足以让我拿到博士学位。有了这个安全保障，我就有可以自由的去寻找并拿下一个重大但有风险的项目了。随着对Sheetz/Spudich试验不断的接触，我的机会来了。从我最后一刻决定去Woods Hole开始，轴突运输项目对我来说整个就是一场冒险。当把科学当做一场伟大的冒险，整个事情就变得有趣了，无论是你的科学成果还是你的个人事业，会有很多意想不到的事情发生。

In my first two to three years in Eric Shooter's lab, I published a couple of papers that were solid but not

outstanding, but I knew that they were sufficient to get a PhD.With that safety net, I had the freedom to lookfor and take on an important but risky project.That opportunity came along with the chance to build upon the Sheetz/Spudich experiment.The whole axonal transport project was anadventure, beginning with a relatively last minute decision to go to Woods Hole. Thinking of science as a grand adventure makes it fun and allows unexpected things to happen, interms of both scientific outcomes and your personal career,

04. 读文献很重要，但不要让它成为你的束缚.

Read the literature but don ’ t be crippled by it.

进入一个新领域，因为其悠久的历史和大量的研究文献，难免会让人显得底气不足，畏手畏脚。这时你必须对先前的工作有一定的了解，但一定要避免陷于各种各样先前试验，掉入按照既有模型进行思考的陷阱。新鲜的视角，和一点很傻很天真的童心会很有用。我刚接触这个领域时，当时轴突的快速运输文献已经很多，但其机理尚不清楚。然而，Allen，Brady和Lasek视频显微镜研究成了关键的转折点，因为它们提供了一种成像小运动囊泡的新方法。未来，通过生物化学来建立这种方法变得可行了，而在此之前，药理学主导了整个工作。 It can be daunting to enter a new field because of its considerable history and litera-ture. You have to be knowledgeable about prior work, but it is also good to avoid getting caught in the trap of doing variations of prior experi-ments and thinking along the lines of existing models. Fresh eyes and some na ï vet é can be a good thing. Fast axonal transport at the time had a long literature but relatively little clar-ity on the mechanism. The Allen, Brady and Lasek video microscopy studies, however, were a turning point because they provided a new way to image small moving vesicles . Going forward, it made sense to build upon that method by doing biochemistry and not stick-ing to pharmacology, which had dominated work in the past.

05. 出好成果不一定要有顶级实验室.

You don ’ t need afancylab to do good science.

我的实验室在斯坦福大学的一个相对较新的大楼中，它有些陈旧却井然有序。而位于海洋生物实验室中的Tom Reese的研究室则相对较乱，在Loeb大楼的地下室的一个小房间中，只有一台化学试剂单放机和一些铺满设备间的小设备。我们在被海水熏的潮湿的地下室房间中解剖乌贼巨轴突。我们戏称这个小房间为“ 海王星的洞穴 ”。但是这一切都没有产生负面影响，相反，与那些在现代大楼中流行的井然有序却单调的实验室相比，这个实验室让人耳目一新。Tom的实验室有符合目前水平满足基本工作需要的设备-------视频灯和电子显微镜。但是在对驱动蛋白提纯的初始阶段，我们楼里没有离心机，所以我们不得不到马路对面的楼中去进行这一步，那时也没有色谱分析设备。但是，一个人可以适应任何环境然后使其正常运转。这也是科学探险一部分。 I came from a pristine, well-organized laboratory in a relatively new building at Stanford. Tom Reese ’ s lab at the Marine Biology Laboratory, in contrast, was a chaotic rabbit warren of small rooms in the basement of the Loeb building, with a monolayer of chemical reagents and small equipment covering most of the available bench space. We dissected squid giant axons in a wet and dank seawater room in the basement, which we called ‘ Neptune ’ s cave ’. But none of this mattered, and it was a refreshing change from the well-organized rows of monotonous lab benches that popu-late most modern research buildings. Tom ’ s lab had state-of-the-art equipment that proved essential for the work—video light and electron microscopy. But at the start of the kinesin puri-fication, there was no centrifuge in the building(we had to go to a building across the street)and no chromatography equipment (we ini-tially used syringes with glass wool). One can adapt to any surroundings and make things work. This also adds to the scientific adventure.

06. 玩命工作，尽情玩耍.

Work hard, play hard and squeeze in time to do your laundry.

科学不是朝九晚五的工作。在Wood
Hole时，我工作异常努力。1984年的整个冬季，我几乎都在工作(Woods Hole的冬天本来也没啥可干，所以我也没有多大损失)。攻坚时刻需要加倍的努力，我很高兴，在关键时刻我花了尽可能多的时间在实验室，见证了科学奇迹的发生。但是，在接下来的春天，我需要离开一段时间来调整状态，所以我骑车游行了欧洲。在到UCSF工作前，我还在尼泊尔和日本玩了四个月。科研关键时刻的攻坚十分重要，就如同打仗时攻克关键要塞。但与此同时，你也必须花时间来平衡你的生活。 Science is not a9-to-5 job. I worked very hard on the projects at Woods Hole; during the winter of 1984, I pretty much only worked (there was not a lot to do during the winter at Woods Hole, so I was not missing much). Special times require special effort, and I was incredibly happy spending as much time as I could in the lab and seeing the science come together. But later in the fol-lowing spring, I needed time off and went on a long bike trip in Europe. I also spent four months in Nepal and Japan before starting my job at UCSF. It is crucial to push a project hard at some points, but you also must make time to balance your life.

07. 坚持比才华更重要.

Persistence is more important than brilliance.

如果你不是天生聪慧(就像我)，只要你能坚持，一样可以在实验科学中做的很好。反过来就很难说。举个例子，在1984年夏天的大部分时间里，因为一系列的实验失误，我未能在体外重建轴突运输。眼看夏天就要结束，我马上就要离开，开始我的见习医生生涯。关键时刻，实验却毫无进展，或许这时，该去休息，去海边的沙滩放松放松。但我并没有这样做，这也许是我在kinesin的故事中，唯一值得赞扬的地方。在我回到斯坦福之前，我近乎执拗的坚持完成这个实验。接着，在度过了神奇的一周后，一个见证奇迹的夜晚降临，一切都是那么的顺理成章。于是，我取消了我的返程航班。 If you are not naturally brilliant (my case), you can still do well in experimental science if you are persistent. The converse is harder. As an example, for much of the summer of 1984, I failed to reconstitute axonal transport in vitro, mostly owing to a series of experimental mistakes. The summer was drawing to a close and I was soon off to start my medical clerkships. With no success up until that point,it might have been a juncture at which to relax and spend time at the beach. Perhaps the only point to my credit in the kinesin story is that I did not take this path. I was dogmatic about giving this experiment my best shot before returning to Stanford. Then, one magical night followed by one magical week, everything came together. I cancelled my return flight.

08. 谁都会犯错.

No project or career is immune from mistakes.

尽管1983 - 1985年期间取得了成功，但它在科学上并不像看上去的那么完美。我们犯了一些概念上的错误和技术上的错误。幸运的是，这些错误并不致命，没有让我们偏离正确的轨道太远以致脱轨。这或许对那些课题不是一帆风顺的同学是一个安慰;时时的困惑，怀疑，对任何课题来说，都再正常不过了。同时，你也会错过很多机会。那时，我们指出“ 溶液中的微管之间也相互作用，形成一个收缩的微管聚合门 ”8(现代术语：一个‘ aster ’)这个论点，但是我们并没有就此研究下去。运动蛋白对微管的自组织作用后来成为一个重要的研究领域。在美国国立研究院对我的

第一次资助中，我还想以“存储”逆行轴突运输的纯化(像是一种叫做HMW 1的atp酶)，作为我获得NIH资助的第一个项目，事实证明这并不是一个明智的决定。职业生涯的每一步都不可避免的混杂着不良决策和英明决策，你只要保持后者比前者多就行了。

As successful as the 1983 – 1985period was, it was not as scientifically perfect as it may appear. We took some conceptual wrong turns and made technical mistakes. We were fortunate that they did not derail us too far off the track. Perhaps this will be comforting to stu-dents whose projects may not be going forward in a straight line; moments of confusion and doubt are typical for any project. There were also plenty of missed opportunities. We noted that“microtubules in solution also moved rela-tive to one another to form a contracted aggre-gate of microtubule”8 (in modern terms, an‘aster’) but did not pursue it. Self-organization of microtubules by motor proteins later became an important area of research. I also thought to‘save’the purification of the retrograde axonal motor (most likely the ATPase called HMW 1) 8,9 for an aim in my first NIH grant,which turned out not to be a sensible decision,as I was scooped before I had the chance to do it. Every career is marked by poor and by good decisions; you just have to try to keep the score-card favoring the latter category.

09. 莫对改变人生计划感到惶恐.

Don’t be afraid to change your life plans.

我二十岁和三十多岁早期时的人生是被规划好的。MD-PhD项目后，最大可能是去医院实习，然后跟大部分人一样成为一名住院医师，然后再回到科学领域。然而，Woods Hole的出现改变了我的人生规划。回到医学院?从我现在的观点来看，答案当然是否定的。但是那时，其他人会怎么说呢?我的导师鼓励我继续坚持自己的课题并延迟医学实习;很显然，我的心思一直在科学上，科学生涯将使我感到快乐。许多年后，单核马达对医学产生了影响使我感到极其满意，同时，针对这种蛋白的药物也正在研发中也是我倍感欣慰。 My twenties and early thirties could have been on autopilot—an MD-PhD program most likely followed by an internship and residency and a later return to science. However, the in vitro motility assays from Woods Hole threw a wrench into that plan. Return to medical school? Certainly not now from my point of view, but what would others say? My mentors encouraged me to stick with the project and defer my clerkships; Stanford Medical School was incredibly supportive, as well. I never returned to medicine; it became abundantly apparent that my heart was in science and that a scientific career would keep me happy. Many years later, it is gratifying to me that molecular motors are having an impact on medicine and that drugs are being developed that target these proteins.

10. 科学发展太快：要坚持做时代的弄潮儿.

Science is moving fast: hold on and enjoy the ride.

作为研究发现的亲历者是非常棒的感觉。但更大的乐趣是，你正在科学的大舞台上，亲眼目睹着科学作为一个整体所取得的惊人进步。科学家是非常幸运的，因为我们能站在世界的前沿，是巨大进步的见证者。科学冒险有许多形式，在实验室的任何一天都有可能“拥抱”微小却美妙的发现。在未来的某一天，某个巨大的惊喜最终到来。永远相信美好的事情即将发生。

It is nice to make your own discovery. But there is also great pleasure in having a seat in the big scientific arena and watching the amazing progress that is taking place overall. As an illustration, I was capti-vated by watching kinesin move vesicles or plastic beads, but it seemed hard to imagine in1984 how one would be able

to understand the detailed inner workings of a motor so small. At that time, I could not envision the many new tools that would come along (single-molecule techniques, better structural methods, genomic studies of a multitude of kinesins) and the ideas contributed by the many people who would enter the field. In the subsequent two decades,we know of many kinesins and the many roles they play and have reasonable ideas of how they produce motion. This incredible progress is being played out in all areas of the life sci-ences, and we scientists are fortunate to have a front-row seat and witness the tremendous advances that are taking place.

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