Run your lab on dollars a day!

Making the move from a postdoc to establishing your own lab can seem daunting. **Jeffrey Perkel** talks to several young researchers and learns the ropes of start up packages, hiring personnel, and how to stretch those funds in the early years.

After years of training and toil, long nights and cold pizza, the big day finally comes: You've been offered a tenure-track position to do research at a university. Now comes the fun part: negotiating your startup package, and planning your future lab.

It's a critical moment in the life of a scientist. A startup package is not the scientific equivalent of an NBA star's signing bonus — it's an investment on the part of the university, intended to prime the pump of your nascent lab and make it self-sustaining.

"As an assistant professor the startup package is intended to fill your lab, allow you to buy equipment, and provide you the wherewithal to attract research funds," explains Adam Zlotnick, a professor of molecular and cellular biochemistry at Indiana University. It's an investment that's good not only for the researcher, but for the university itself. If a faculty member fails to get tenure because their startup was too small, he says, "all that money went down the drain."

"Independent of whether or not that person was good enough to receive tenure, if they were starved to death for money, then they won't thrive and the university has cut its own throat."

Details vary, but startup packages generally provide funding for big-ticket items as well as your pipettors, your computers and reagents, travel, personnel and so on. How generous the package is, of course, varies by school, discipline, and other intangibles. But one thing is certain: However large it is, there will always be something you will need but cannot yet afford.

When you need that big-ticket item

For Bernd Bodenmiller, that something, or rather, those somethings, are mice.

Bodenmiller was a postdoctoral fellow at Stanford University with Garry Nolan when he was offered a group leader position at the Institute of Molecular Life Sciences at the University of Zurich in 2011. While at Stanford, Bodenmiller, who officially started in Zurich on February 1 of this year, mastered a relatively new piece of equipment, a CyTOF mass cytometer from DVS Sciences. The CyTOF is like a flow cytometer, but rather than nondestructively enumerating and characterizing fluorescently labeled cells, the CyTOF "nukes" them in a mass spectrometer, quantifying cellular antigens by the abundance of lanthanide-tagged antibodies.

Bernd Bodenmiller, group leader at the Institute of Molecular Life Sciences at the University of Zurich

The CyTOF enables multiplexing levels unheard of for standard flow cytometry instruments; Bodenmiller has run assays with some 35 distinct tags (or "channels") to tease apart cellular signaling pathways. An experienced flow cytometrists might top out at 10 or 12.

Zurich didn't have a CyTOF, so naturally that instrument, which costs some \$650,000 to \$700,000, represented a key component of Bodenmiller's startup package. "It was essential to get a CyTOF instrument for my own research group, as everything I'm doing is surrounded by the technology of mass cytometry," he says.

Bodenmiller's package included a million dollars for equipment, reagents, and consumables, plus approximately \$200,000 per year for six years for personnel — \$2.2 million in total. And, in what should come as no surprise, much of the equipment budget is already spent. In addition to the CyTOF, he used his money (plus some additional extramural funding) to purchase such standard lab items as pipettors, centrifuges, vortexers, refrigerators, and so on. He'll also need argon gas — the CyTOF requires a steady supply, between \$10,000 and \$20,000 per year, he estimates — as well as a service contract (typically about 10% of the purchase price of an instrument). And then he'll need antibodies, each of which can cost from \$500 to \$1,000 apiece, plus the reagents to couple them to their lanthanide tags (\$3,000 for up to 40 reactions).

Bodenmiller says his \$200,000 annual budget is enough to support up to two postdocs or four graduate students. He plans to start with two graduate students

and a technician, though — a small group of individuals he can train carefully who can then help train others as the lab grows. Postdocs, he says, will come later, once he's figured out what new expertise (such as bioinformatics) he'd like to fold into the lab.

Certainly, Bodenmiller is well off, financially speaking, for such a young faculty member. Yet he does have limitations. Nolan's lab, for instance, had dedicated robotics facilities and bioinformatics expertise. But Bodenmiller doesn't yet have the money for such things. Instead, he will access them either via the university's core facility or collaborations with other researchers. The same is true for mice, as the per-diem cost of maintaining a mouse colony can quickly drain a lab's reserves.

"For the first couple of years, certainly my focus is getting the CyTOF up and running and be very productive with it. And then I can think [about] what are the next steps," he says.

Ultimately, of course, Bodenmiller may need to establish a mouse colony of his own, but that won't be for several years, by which point he should have additional funding, more personnel, and more in-house expertise.

"If it's about making tough decisions, then certainly every young group leader has to make them," Bodenmiller says. Yet a collaborative environment can make a big difference. Senior faculty at Zurich often help young investigators by sharing equipment such as PCR machines and tissue culture hoods, so they can see what they need prior to purchasing it. "This can help a lot so that young groups can be very quickly productive," he says.

The fish lab

R. Craig Albertson has actually negotiated and received two startup packages during

Adam Zlotnic, professor of molecular and cellular biochemistry at Indiana University

R. Craig Albertson, assistant professor of biology at the University of Massachusetts, Amherst

his relatively young career. Albertson, who joined the faculty at the University of Massachusetts, Amherst, as an assistant professor of biology in July 2011, had held the same position at Syracuse University since 2006. Before that, he was a postdoctoral fellow in Boston.

"I'm kind of a New Englander at heart," Albertson says.

Albertson is an evolutionary biologist who studies the impact of genetic variation on phenotypic variation in fish — specifically, zebrafish, as well as another class of tropical fish called cichlids.

These fish are housed in 20 40-gallon aquaria, 20 10-gallon aquaria, and 100 smaller 3L tanks, with dedicated pumps, filtration systems, lighting, and so on. Not just any room can house that much equipment — the room needs to be large enough (800-plus square feet) to comfortably hold all the tanks and associated hardware, have floor drains installed, and most importantly, be structurally equipped to handle the point loads of that much weight. Naturally, animal facilities turned out to be the key deal-breaker for Albertson, both at Syracuse and in Amherst.

Albertson estimates the equipment in his fish room cost about \$100,000 or so, plus another \$25,000 for the installation. He was able to save some money by moving much of that hardware over from Syracuse, paying the university just 30 cents on the dollar for equipment that was only four or five years old. That was "a pretty good cost saver," he says — though perhaps not as good as it sounds on the surface: He had to pay an additional \$30,000 to disassemble,

move, replace broken or worn equipment, and reinstall everything.

Most other lab gear he purchased anew, including microscopes, digital imaging equipment, computers, and centrifuges. He estimates that in the six months since he joined the department at University of Massachusetts, he's spent about half of his \$400,000 startup package. "Money is flying out of the lab now," he says.

Part of that outflow is because of research expenditures. A comparative whole-genome next-generation sequencing analysis of some 300 individuals from Albertson's collection, being outsourced to Oregon-based Floragenex, will cost nearly \$40,000 for the raw sequence, plus another \$5,000 for a computer to process the data. Transcriptome sequencing studies are running between \$5,000 and \$6,000 apiece. And then there's the post-sequencing functional validation assays using antisense morpholino oligonucleotides, each costing about \$500.

But the lion's share of his money has been earmarked for personnel. Albertson has two postdocs and two graduate students in his lab, which he supports from both his startup funds as well as grants from National Institutes of Health (NIH) and National Science Foundation. He would like to add to his group, but that's just not practical at the moment, he says, as it is simply no longer possible to hire workers for a year at a time with the expectation that funding will naturally follow. "You really need to commit to, in my opinion, at least two years to a postdoc in order to provide enough time for them to secure funds on their own," he says.

Everything old is new again

That two-year minimum is a recurring theme, and it's one that ties Indiana University's Zlotnick's hands as well. Zlotnick, like Albertson, is on his second startup package. But he didn't come to IU as a fledgling faculty; Zlotnick had spent 10 years at the University of Oklahoma Health Sciences Center, rising to the rank of full professor before making his move in 2008.

As a more experienced researcher with a distinguished record of grantsmanship and publication, Zlotnick found himself in a better position than when he negotiated his first startup package. That's because startup packages awarded to young faculty are intended to help those researchers get up and running, while for more senior faculty, "the university is trying to attract you, as opposed to just get you going," says Zlotnick. He declined to divulge the details of his own startup package.

Zlotnick, a biophysicist who studies viral assembly, says he moved to Indiana because of its opportunities for collaborations, a larger graduate student body, as well as lifestyle. "Bloomington is the archetypical Midwest college town," he says. "It's the kind of town in central Indiana where you have your choice of Tibetan restaurants."

A more practical reason might have been IU's structural biology resources. The university has a cryo-electron microscope (EM) on-site, which Zlotnick uses for his structural studies of viral proteins. "If I were to buy a new EM, I would have to spend about \$2 million and worry about personnel to maintain it," he says. Instead, he borrows time on a shared instrument that costs him just \$50 per hour. IU is also a member of a consortium supporting a beam line at the Advanced Light Source (Lawrence Berkeley National Lab) and is just a five-hour drive away from the Advanced Photon Source at Argonne National Laboratory in Chicago. Use of the former costs just a few hundred dollars to ship frozen samples cross-country. The latter is basically a road-trip, with free instrument access offset by an estimated \$700 to \$1,000 per experiment for "car, hotel, and food."

When he moved to Indiana, Zlotnick was able to move some of his old lab's hardware, but he had to leave a lot behind, as well. Among his new purchases were a spectrophotometer, fluorimeter, water-purification system, incubators, and chromatography equipment — standard fare for a biophysical laboratory, all of which cost several hundred-thousand dollars.

Yongsheng Shi, assistant professor of microbiology and molecular genetics at the University of California, Irvine

Yet with 11 people in the lab — one full-time and one part-time technician, five postdocs, and four grad students — Zlotnick spends most of his budget on personnel. Postdocs cost nearly \$70,000 per year when accounting for salary fringe, and supplies, and like Albertson, Zlotnick says he won't hire someone unless he can support them for at least two years. When it comes to investing money, he says, "It's really the hands and minds that do the work. And those are just as expensive as they can be."

Going genomic

Personnel also weigh heavily on Yongsheng Shi's balance sheet. The young assistant professor of microbiology and molecular genetics at the University of California, Irvine, studies the impact of messenger RNA processing on cancer development and stem cell differentiation. To do that, Shi mixes biochemical and genomic technologies, funding the former with an NIH RO1 grant and the latter off his startup. That package, Shi says, amounts to between \$600,000 and \$700,000 for equipment, reagents, and salary costs.

With that money, he's purchased everything from pipetmen and microcentrifuges to biosafety cabinets and -80 °C freezers. But again, the bulk of Shi's money pays for his technician, graduate student, and postdoc (plus a fraction of his own salary).

"I spend definitely more than half of the money on salaries," he says. Indeed, the rule of thumb is that each lab member consumes between \$10,000 and \$15,000 per year on reagents and supplies, plus another \$50,000 to \$60,000 in salary and benefits. That comes to \$60,000 to \$75,000 per person per year, meaning Shi's lab spends as much as \$300,000 annually on salary and reagents

alone. His RO1 supplies about two-thirds of that cost with his startup package providing the rest for now. "That's how I can make ends meet," he says.

But of course, startup funds are neither infinite nor renewable. As a result Shi, like all researchers, has to think long and hard about any new hires. In particular, he would like to hire a bioinformatics specialist, but in the absence of a new grant, such a position would necessarily have to be for no more than two or three years. "Without additional funding, I won't be able to support them for longer than that."

Shi also has had to make some hard decisions on the experimental front. He's spent quite a bit over the past year on next-generation sequencing experiments. His team developed a method to use Illumina sequencing to monitor mRNA polyadenylation, but at the moment, that project is not yet grant-funded. Each lane cost between \$1,100 and \$2,000, consuming at least four lanes per experiment. His lab ran some 10 to 20 samples in 2011, he says, costing between \$20,000 and \$40,000. Add in the cost of sample preparation, and his lab spent some \$50,000 on sequencing alone. "I would love to do more [sequencing], but we have to do what we can, not exceeding the budget too much," he says.

And then there's cell culture work. Shi works with mouse embryonic stem cells, and would like to grow them in bulk for protein purification. Unfortunately, mESCs require expensive sera and growth factors like leukemia inhibition factor (LIF) to grow, and he simply cannot afford it.

His solution is to use a stem cell "surrogate" — a cell line whose behavior mimics that of stem cells, but that can grow in the absence of LIF. P19 rat cells, for instance, exhibit some of the characteristics of stem cells and can also be induced to differentiate, albeit not in quite the same way, or with as much plasticity, as stem cells.

"You have to sacrifice sometimes," he says.

When it comes to getting a lab up and running, *sometimes* occurs more often than not.

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