CELL MATES

Collaborations are more integral to the life sciences than ever — and funders are trying to keep pace. **Jacqueline Ruttimann** reports.

Gaudenz Danuser is an associate professor at the Scripps Research Institute's cell-biology department in La Jolla, California. But he is not a cell biologist — Danuser was formally trained as an engineer. In the past, when he jointly applied for funding from the National Institutes of Health (NIH) to study mathematical modelling of cellular processes via the agency's standard R01 grant, Danuser would have to come to an agreement with his cell-biologist collaborator, as only one could lead the grant. But a new programme at the NIH has made his task easier and potentially more professionally rewarding. The NIH has set up a multiple principal investigator (PI) grant, which means that Danuser can get official recognition for his efforts. Previously, he says, "I was at the mercy of my friends to give me the money."

"The NIH has really taken the lead in putting administrative structures into place that will both recognize and nurture collaborations," says Mary Beckerle, former president of the American Society for Cell Biology and current member of NIH director Elias Zerhouni's advisory committee. Crediting multiple researchers is especially helpful for young tenure-track PIs looking to log experience as independent researchers on their curricula vitae, she says. Failure to document such accomplishments could "have ramifications for his or her academic survival", says Beckerle. Recent fraud cases have highlighted the need for co-authors to be clear about accountability (see *Nature* **450,** 1; 2007).

Crossing boundaries

Interdisciplinary collaborations are encouraged by numerous interdisciplinary institutes and centres, and are becoming increasingly common — there were five times more scientific papers with international co-authors in 2005 than in 1985, according to recently released figures from the Organisation for Economic Co-operation and Development. But finding the right funding agency, and the right funding category within that agency, can be a challenge.

Danuser and his collaborator Peter Sorger, a systems biologist at Harvard University, are two of the first recipients of a multi-PI grant. They are seeking to combine advanced image analysis and genetics to study proteins in the cell-division complex known as the kinetocore. Sorger welcomes the new grant.

"It allows you to fund new things you couldn't do otherwise, identify more easily who's doing what and figure out if the collaboration was a success," he says. But he is concerned that the NIH should not view multi-PI grants as a way to save money, as the total amount is the same as that of the single-PI grants: the NIH would be "paying less to fund the same science".

Still, Sorger sees the grants as a positive step. "Science has a long history of recognizing and glorifying individual achievement," he says. "We need to move to a more sophisticated way in which collaboration is recognized, but not to the detriment of the individual." Sorger likens collaboration to a strong marriage. "It doesn't just happen, you have to work at it," he says.

"Glue grants are an experiment into how to support science. Other investigators may feel threatened."
— Jeremy Berg

Indeed, the challenges are many. Despite the success of the NIH's interdisciplinary Specialized Programs of Research Excellence (SPORE) grants — started by the National Cancer Institute in 1992 — there have been pitfalls. SPORE grants have one director who oversees a minimum of four research projects, each of which has two co-leaders: one for basic research and one for clinical research. The grants, which target translational cancer research, require a clinical trial at the end of five years. It's been a tough target to meet. And when the $2.5-million-a-year SPORE grant is divided up among all participants, it works out to less than the average R01 grant, which is typically $220,000 a year. Even so, the grants have led to 120 phase I and phase II clinical trials and the identification of 110 biomarkers.

Similar challenges persist with the NIH's 'glue grants', so called for their effects in holding a disparate group together. These large-scale awards, initiated in 2000, bring together groups of scientists from different fields to work on a project that lasts up to 10 years and is outside the purview of a traditional R01.

Groups could have difficulty maintaining the resources that have been created once the grants have expired, says Jeremy Berg, director of the National Institute of General Medical Sciences, which started the grant. Then there's the need to find a balance between those investigators on the glue grant and the larger group of others active in the same field. "Investigators may feel threatened by the competition due to the activities of the glue grant," says Berg, who acknowledges that the NIH is actively working to explore these issues.

Berg cites glue-grant successes such as the Consortium for Functional Glycomics, through which a large collection of biologically relevant carbohydrates known as glycans has been collected or synthesized and presented on arrays. Investigators can submit requests and get help to have their samples screened against these

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arrays. The results are made public via the Internet, enabling other scientists to mine the data for general patterns relevant to cell–cell and other interactions.

Collaborations can make judging grant applications tricky. Funders of collaborative interdisciplinary research must ensure there is broad enough expertise among reviewers of proposals, points out Nicola Perrin, policy adviser at biomedical charity the Wellcome Trust. The trust's awards scheme encourages interdisciplinary research collaborations involving basic scientists, clinicians and non-biologists such as mathematicians, physicists, chemists, engineers and social scientists. Wellcome also funds interdisciplinary centres such as the Wellcome Trust Centre for Cell-Matrix Research at the University of Manchester, UK, which is currently running projects on matrix assembly, adhesion signalling, cell-fate determination and tissue regeneration.

Interdisciplinary translational research projects sometimes have a hard time making it to the clinical-trials stage in a timely manner, says Richard Seabrook, head of business development in the Wellcome Trust's technology-transfer division. To circumvent this, the trust provides advisers to help guide projects on at different stages in their lifespan. Even just articulating a project to funders — given the work's multifaceted, cutting-edge interdisciplinary bent — can be a challenge, says Seabrook. From January 2008, to help people communicate a project's method and objectives, the Wellcome Trust plans to include presentations as part of the grant-application process for translation awards.

After some disappointing early results, the Human Frontier Science Program Organization (HFSPO), an international consortium supporting multidisciplinary research, had to alter its review process for its multi-country grants. Geoff Richards, director of research grants, says that many of the first grant applications paid only lip-service to the interdisciplinary mission. "The review committees have learned to spot projects that contain thinly disguised add-ons," says Richards. The three-year grants fund basic research. Applicants must have a lab in one of the HFSPO's member

T. PIOTROWSKI

"Scientists return to developing countries, bringing this culture of collaboration with them." — Alejandro Sánchez Alvarado

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countries, which include most European countries, India, Japan, South Korea, Australia, New Zealand Canada and the United States.

Initially, many HFSPO grant applicants had team members often chosen more for their geographical location than for any real contribution they could make to the project, Richards says. By including committee members from, for example, chemistry, physics and biocomputing, he says the programme has developed a review culture that spots most of the cases in which team members are poorly integrated into the proposal. To level the playing field, HFSPO grants are divided into two separate categories: one for teams of young researchers starting out and one for researchers at any stage of their career.

Taking it home

Scientists in the developing world are often eager for collaborations, but can have difficulty finding the right mechanism. Venezuelan-born neurobiologist and Howard Hughes Medical Institute investigator Alejandro Sánchez Alvarado, of the University of Utah in Salt Lake City, thanks the Millennium Science Initiative (MSI), partly funded by the World Bank, for helping him collaborate with scientists in Latin America. The initiative aims to help scientists and engineers from the developing world to do top-level research in their own countries. As Latin American scientists who trained abroad move back home to work in these specially designed research centres, he says, they are "bringing this culture of collaboration with them". Scientists working at MSI centres are encouraged to work both in the public and private sectors, inside and outside their own fields.

Cooperation is key to the success of these large efforts. A weak investigator could potentially hide behind a strong one (see *Nature* **437,** 590–591; 2005). Or burnt-out investigators could join less senior scientists solely to tap a funding resource. The multi-PI grant could help get around such pitfalls, by making it harder for one person to represent a large group.

Proper collaboration may have to come from the ground up. "I don't think you can force collaboration top-down by having grant mechanisms," says Danuser.

But the bodies that find effective ways to support interdisciplinary collaborations are likely both to gain recognition and attract expertise. "Institutions need to remain flexible and nimble as the face of science changes," says Beckerle. "They need to figure out how to fund the best science with the fewest boundaries." ■

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