ILLUSTRATION BY OLI WINWARD

How team science extends your scope

Modern cancer research demands input from collaborators across a broad spectrum of disciplines — not all of them scientific.

BY NEIL SAVAGE

When Daniel Stover was doing his postdoctoral research in a cell-biology lab at Harvard Medical School in Boston, Massachusetts, he ran into a problem. He was studying a type of breast cancer, trying to work out whether genetic differences between one part of a tumour and another contributed to the cancer's resistance to chemotherapy. He had plenty to work with — genetic information from hundreds of tumour samples — but no idea how to handle it all.

"I had generated an immense amount of sequencing data and couldn't find anybody to analyse it," says Stover, now an oncologist at the Ohio State University's Comprehensive Cancer Center in Columbus. So, with the help of a bioinformatician in the same lab, he started studying computational biology, which became the focus of his studies. "I found that I loved working with data," he says. All the papers he published as a postdoc ended up being based on informatics, and now his own lab, which he set up last September, focuses on clinical computational oncology.

Stover's lab aims to fill the space between the computer experts who develop data-handling algorithms and the clinicians who focus on patient care, treatment and clinical trials. "In between, there's a gap, and we try to fill that void and take these amazing algorithms and apply them in clinical settings," he says.

Stover says the collaboration changed the direction of his career, in part because it gave him new skills that he could apply in working with other researchers.

Cancer research has become highly multidisciplinary. The field now includes not just clinicians and molecular biologists, but also computational biologists, statisticians, nanotechnology experts and chemical engineers. And that creates challenges for all those researchers. How do they work with people who have different areas of expertise, each with its own basic assumptions and specialized language?

Nancy Krunic, who works for Novartis Pharmaceuticals in Cambridge, Massachusetts, heads the company's Future Precision Medicine Diagnostics group, which is developing assays, software and other technology to aid in diagnosis. "No one person or one department, or one lab, is going to have all the tools they need to tackle the problem," she says. "You absolutely

MAKING IT WORK
'Prenuptial agreements' for scientists

To help researchers to collaborate in multidisciplinary groups and anticipate difficulties in a project, the Office of the Ombudsman at the US National Institutes of Health came up with what it calls a prenuptial agreement for research teams. This lays out areas in which teams should reach agreements before problems arise (see go.nature.com/prenups). Here are some of the questions it suggests asking and answering before a collaboration begins in earnest:

- What are the scientific goals and expected outcomes of the project?
- When will the project be over?
- Who will write the reports?
- How will you decide what to do if discoveries made during the project change the direction of your research?
- Who will do the hiring, firing and supervising?
- How will credit and authorship be assigned?
- How will you make decisions about new collaborations or spin-off projects?
- What will you do about patents and intellectual property?
- Who will manage the data?
- What will happen if a collaborator changes job during the project?

need diverse backgrounds and subject-matter expertise."

Whether they're big pharmaceutical organizations or medical-device companies (Krunic previously worked at Luminex Molecular Diagnostics in Toronto, Canada), industry groups targeting cancer must form multidisciplinary teams, Krunic says, if they are to define and tackle problems in ways that are scientifically, clinically and commercially viable. As well as scientists and technologists, these teams will include people with expertise in, for example, marketing and regulatory issues, says Krunic.

BEYOND BIOLOGY

Programmes exist to promote cross-fertilization between disciplines. The US National Cancer Institute (NCI), for example, established a Physical Sciences in Oncology initiative in 2009 to team cancer biologists with physicists, mathematicians, chemists and engineers. Those disciplines come at cancer in a variety of ways. Chemical engineers devise new diagnostics and develop nanoparticles to carry drugs to tumours, or to act as contrast agents that make smaller tumours visible in imaging. Physicists and bioengineers study the effect of mechanical forces on tumour growth and behaviour, and mathematicians develop computational models to explain the complex interplay between different cancer cells, blood vessels, healthy tissue and drugs.

For example, researchers are working to understand the physical effects of a tumour's environment. How does an increase in tumour stiffness affect the shape and behaviour of the cells within it? And when a metastasizing cell deforms to squeeze through tight spaces, what does the increased pressure do to the cell's nucleus — does it, for instance, trigger processes that damage DNA? "It's not just the physical forces, but that's an important aspect of what's being studied," says Nastaran Zahir, director of the Physical Sciences in Oncology programme. Other projects include applying mathematical approaches such as game theory to determine dosing strategies that will minimize the development of drug resistance, instead of applying the standard 'maximum tolerated dose' approach.

Zahir has experience of crossing disciplines. She earned her bachelor's degree in nuclear engineering, and studied plasma physics before moving into radiation biology and getting her PhD in bioengineering in a cancer research lab. So she's aware of the difficulties. "Biology has its own culture. Physics has a different culture," she says. "In physics, what you search for is sort of the ultimate truth — is there a law? But biology's very messy, and you don't necessarily have an exact process." Because biological processes change in response to new stresses, it's difficult to come up with laws for how a targeted cell would react to a cancer drug, for example.

LANGUAGE BARRIERS

To help bridge such gaps between disciplines, the NCI created the Science of Team Science programme. Kara Hall, a behavioural scientist who directs the initiative, says it's important for people to share knowledge with those from other disciplines in a comprehensible way. "That entails reducing the jargon that's being used, or finding ways to define that jargon as you go along," she says. It is often helpful to use analogies to explain key concepts in a field. It's also useful for researchers to engage in 'team learning', in which individuals are tasked with gaining in-depth information on a topic and bringing it back to their colleagues. Hall says teams should reflect on how well they function, by discussing, for instance, whether their meetings are sufficiently frequent and informative.

Hall says that people must be open when they approach specialists in other fields. It's important, she advises, to practise 'disciplinary humility' — to realize that all disciplines have both strengths and weaknesses, and to be willing to learn from fields other than your own. Finding a safe common ground to ask questions can be difficult. "If I'm a psychologist collaborating with a geneticist, I may be afraid to ask a 'genetics 101' question because I might be seen as intellectually inferior," Hall says.

Other challenges in team science include the need for extra planning and management time, compared with individualized research. The approach can also require more team meetings and more travel, when collaborators are located across campus or at other institutions. And some institutional structures have not yet caught up with the concept, Hall says. Promotion and tenure committees tend to look mainly at the first and last authors of papers, she says. And that means they might not recognize how much a middle author has contributed — even though, in teams, middle authors play a crucial part in the research. Yet, Hall says, her programme's surveys found that trainees who had worked in multidisciplinary teams reported that their experiences had made them more competitive in the job market.

Defining the goals of a project, planning its implementation and working out in advance how to resolve conflict are all important parts of setting up a collaboration. The NCI offers the Team Science Toolkit, an online resource whereby researchers can share information and post news about funding opportunities and job openings (see go.nature.com/tstoolkit). It also helps to plan and support an annual Science of Team Science conference, which focuses on ways to make team-based research more effective. The next meeting runs from 21 to 24 May at the University of Texas Medical Branch in Galveston. And the US National Institutes of Health offers what it calls a "prenuptial agreement" to help scientists prepare for problems that can arise during a collaboration (see 'Making it work').

One early-career researcher taking a multidisciplinary approach is Viktor Adalsteinsson, who leads the blood-biopsy team in the cancer programme at the Broad Institute of MIT and Harvard in Cambridge. Although he earned his doctorate in chemical engineering, in 2015, Adalsteinsson knew from a young age that he wanted to help cure cancer. He did his PhD work at the Koch Institute for Integrative Cancer Research, which was set up at the Massachusetts Institute of Technology to bring biologists and engineers together under one roof. He helped to develop a system to isolate and sequence circulating tumour cells from blood samples, using his chemical-engineering education to deal with issues such as fluid dynamics and the amount of shear stress that cells could handle. Now in his own lab, he's trying to capture cell-free cancer DNA from blood to perform sequencing for precision medicine, reducing the need for invasive biopsies.

One of the ways in which Adalsteinsson and the people he works with stay up to date is through frequent meetings and seminars, at which various specialists talk about their work. Having a network of colleagues who can explain research from other disciplines, or tell him whether a journal article is significant, is helpful, he says. "It's impossible to be an expert in every possible area, and knowing when to turn to others is really important."

POOL EXPERTISE

Sometimes the trick lies in knowing what not to read. "Being able to scan and reject a bunch of stuff is really important," says Heather Parsons, a medical oncologist and physician at the Dana–Farber Cancer Institute in Boston, who specializes in breast cancer and its biomarkers. She, too, emphasizes the importance of having a network of experts, developed through university and work, with whom you can discuss questions.

Parsons collaborates with Stover and Adalsteinsson on the liquid-biopsy work. "I like very much being part of this kind of a team," she says, "but it requires that you don't have an enormous ego and you don't mind asking about things you don't understand."

At Stanford University School of Medicine in California, Guillem Pratx gets members of his physical oncology lab to take part in a journal club. They meet for an hour or so to focus on a particular paper, allowing people from different disciplines to gain a good understanding of its importance. He also requires them to attend meetings outside their field to broaden their knowledge. With enough exposure, he says, scientists can become comfortable with the terminology and concepts used in other areas. "I notice the more I sit in these talks, the more I understand," Pratx says. "It's like learning a new language."

Pratx did his undergraduate and graduate studies in electrical engineering, and during his PhD studies he worked in a radiology lab, using graphics techniques from computer games to improve the processing of medical images. He did his postdoctoral research in radiation oncology, and he feels that using postdoc time to learn about an area outside one's core speciality can pay off. It can be difficult to be hired by a lab that specializes in a field far removed from yours, he acknowledges. But if there's some overlap, it can add valuable expertise.

Pratx's lab, which includes scientists with backgrounds in physics, engineering, chemistry and biology, develops instruments, probes and algorithms for cancer imaging. The team is studying how the luminescence generated when therapeutic radiation hits tissue can be used to carefully aim the otherwise-invisible beam. One challenge for such multidisciplinary teams is communicating to different members how they can tackle a problem, he says. Biologists often struggle to understand what questions mathematical models can ask concerning the large data sets generated in cancer research — sets that include not only genomic and proteomic sequences, but also imaging results and environmental information from medical records. It's important that there's someone in the group who understands which statistical methods are best applied to particular types of data, and what the results do and don't show, says Pratx.

On the flip side, he thinks that engineers can focus too much on trying to come up with innovative techniques, and are sometimes less interested in applying what others have already developed. It's not enough for insights gleaned from data to be new, he says. They also have to be biologically relevant.

One problem that Pratx sees is the one Stover experienced. Although the growth in data is increasing the need for computational specialists in cancer research, the competition from other fields for people with those skills is strong.

MATCHMAKERS

Early-career researchers interested in forming collaborations need to network with people from other fields, and one obvious way is to attend conferences in those fields. But Jennifer Podesta, a molecular biologist and a specialist in the use of nanotechnology for drug delivery, says that simply attending a conference isn't enough. "Do a little bit of homework, and go in very much with an agenda of 'who it is I want to meet and what do I want to get out of it?'" she says. "It's remarkable how many people think they can show up, scrunch over and stand in the corner, and come away from it complaining that they didn't meet a collaborator."

Podesta, who runs the Cancer Research UK Centre at Imperial College London, recommends working out the type of scientist you need for the project you have in mind, and then approaching department heads in your own university to see who they think might fit. Funding managers also tend to have a broad knowledge of which researchers have what expertise, and are usually happy to play matchmaker.

Getting funding for cross-disciplinary projects can be challenging, especially for someone who hasn't yet established a reputation, so Podesta suggests looking for small sums of money internally, to fund a pilot project with a new collaborator. Such projects demonstrate that members of the team can work together and produce viable ideas, making them more attractive to funding agencies. The NCI's Physical Sciences in Oncology programme provides funding specifically for pilot projects.

Trying to keep up with a field as dynamic as cancer research is daunting. "We have so much information within our reach, and new discoveries are being made every day," Adalsteinsson says. The key to tackling all that information, Pratx says, is to overcome the tendency of many scientists to think they need to learn everything themselves. "I think it's an important skill when you're able to say, 'Maybe I don't need to be an expert in computer modelling. I can maybe work with somebody else,'" he says. ■

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