sponge containing halichondrin B, from the deep waters off New Zealand. He also teamed up with researchers to grow more of the sponges, flying seaplanes out to remote aquatic farms where the sponges grew attached to lines dangling 40 metres beneath buoys. The reward for his efforts: just 300 milligrams of halichondrin B, the equivalent of a few grains of rice. "My hair turned white as a result of halichondrin B," he jokes.

Meanwhile, Tokyo's Eisai Pharmaceuticals had licensed the patent on Kishi's method and began synthesizing hundreds of analogues of the compound. Newman's haul from New Zealand was just enough to conduct comparative studies with some of these analogues. One of them, eribulin, is more potent than halichondrin B yet also substantially smaller and easier to make. But it still has 19 stereocentres (see structure, inset), and production of eribulin on a commercial scale seemed unfathomable.

Eisai says that eribulin takes 62 steps to synthesize — a remarkably long process for a marketable drug. The company was initially apprehensive about the project, says Kishi. But once the phase I study results had shown that the drug was safe — and revealed hints of clinical efficacy — "all the reservations disappeared", he says.

Further clinical trials showed that eribulin extends the lifespan of patients with late-stage breast cancer by an average of 2.5 months in those who are not benefiting from other chemotherapies such as Taxol, also a natural-product derivative. Analysts suggest that eribulin could command a US$1-billion market if it is approved for treatment of other cancers.

Few other pharmaceutical companies have been willing to bet on complex natural products. During the 1990s, many largely abandoned natural-product chemistry, focusing more on screening large libraries of synthetic chemicals for drug candidates, says Michael Jirousek, who once worked on halichondrin B synthesis and is now chief scientific officer and co-founder of Catabasis, a biotechnology company in Cambridge, Massachusetts. "Screening natural products and isolating the active ingredients is becoming a lost art," he says.

Proponents of total synthesis point to eribulin as proof that their approach, albeit arduous, can be highly successful. Phil Baran, a synthetic chemist at the Scripps Research Institute in La Jolla, California, says that more young investigators are entering the field and that improvements in chemical techniques are making it possible to synthesize additional complex molecules by commercially viable routes. "As advances in organic chemistry become greater and greater," he says, "I think we're going to see a lot more complex compounds being pursued by companies." ■

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Canada's Perimeter Institute boasts a freewheeling intellectual environment — and a gourmet bistro.

RESEARCH

Physics centre plans rapid growth

Perimeter Institute steps up drive to attract top talent.

BY IVAN SEMENIUK

Newton, Maxwell, Einstein, Bohr, Dirac — the list reads like the ultimate physics dream team. That the Perimeter Institute for Theoretical Physics in Waterloo, Canada, has chosen to name five new research chairs after some of the greatest physicists in history is a sign of its lofty aspirations.

"We're scouring the world for exceptional talent," says director Neil Turok, who took the helm at the Perimeter in 2008. The institute began attracting up-and-coming researchers soon after its creation, but it has had a harder time building into its ranks the experience and scientific prowess to rival more established theoretical centres, such as the Institute for Advanced Study (IAS) in Princeton, New Jersey. The new chairs, announced on 29 November, are designed to attract top theorists in "a gathering of critical mass around the most fundamental questions", Turok says. "Our mission is to make breakthroughs."

This is not the first time a physics institute has announced such an ambitious goal, but the Perimeter's resources give it a better chance than most of achieving it. The institute was founded in 1999 with a hefty personal gift from entrepreneur Mike Lazaridis, whose company, Research in Motion, makes the popular BlackBerry products, and it has grown quickly since then through additional public and private funds.

The faculty now numbers 14 full-time posts and 12 part-time associate posts, with more hirings expected in 2011. Largely spared the commitments that come with an academic appointment at a university, researchers at the Perimeter enjoy an unfettered and freewheeling intellectual environment, together with less cerebral indulgences, including a gourmet bistro and a squash court. The institute has begun to make significant contributions in areas such as quantum field theory.

"The chair holders will be free to engage in investigator-driven research, without limits or mandates," according to a description of the new positions. An Can$8-million (US$7.8-million) endowment has been secured for the first chair, named after Isaac Newton, with half the money provided by the Perimeter's existing endowment and the rest by BMO Financial Group, one of Canada's largest banks. The institute is now seeking partners to fund the remaining chairs.

"The place is really flourishing now," says Nima Arkani-Hamed, a theoretical physicist at the IAS. Despite initial reservations when the Perimeter first opened, Arkani-Hamed now collaborates frequently with colleagues there and has seen growing numbers of IAS students and postdocs choosing job offers from the Perimeter over those from more established institutions. IAS researcher Davide Gaiotto, who will take up a faculty position at the Perimeter next year, agrees that there is no shortage of physics talent to fill the new positions. Others say that privately endowed institutions such as the Perimeter and the Simons Center for Geometry and Physics at Stony Brook University, New York, are helping to keep theoretical physics active while the economic downturn hits public universities in the United States and Europe.

Even a few strategic hirings can have a powerful effect on a field, notes Michael Douglas, a string theorist at the Simons Center. Douglas recalls his time as a postdoc at Rutgers University in Piscataway, New Jersey, when four key faculty appointments in 1989 — the 'string quartet' — led to a collaboration that transformed string theory. "If you choose right," he says, "then things can really take off." ■