

The Howard Hughes Medical Institute (HHMI), headquartered in the Chevy Chase suburb of Washington, DC, is the largest non-profit funding body for biomedical research in the US, with an annual budget of around \$670 million.

Until now, it has been a virtual institute, renowned for sponsoring elite investigators working at over 70 host laboratories around the country. But changes are afoot. HHMI president Tom Cech talked to *Nature Medicine* about his vision for the organization's future.

Thomas R. Cech

We began our discussion with the news that the Howard Hughes Medical Institute (HHMI) is, for the first time, to create a physical campus built on the 281-acre Janeila Technology Park in Loudoun County, Virginia, purchased for \$53.7 million. The new campus will focus on "bioinformatics and the development and dissemination of other technologies that cannot be purchased off the shelf," according to Cech.

If this sounds vague, that's because it is. Laboratories are at least five years away from becoming operational and Cech explains, "There are many technologies that one wouldn't need a new campus for, such as making oligonucleotides or Affymetrix chips—these you can buy. Two years ago, DNA microarrays were new but now they're standard technologies. We're talking about a level beyond that and it's a moving target."

The creation of such a campus is a significant change for an organization that has until now operated by funding researchers within their host facilities. And even though the change will cost more per researcher, Cech says change is needed because the life sciences landscape has changed: "At the time when physics moved to needing big instrumentation and equipment that individual labs couldn't afford, biology was still this wonderful thing you could do in your garage. Now we see things like high-voltage cryo-electron microscopy, which gives an opportunity to look into cells and find out not just where organelles are, but where individual molecules are at any given time. All of this equipment is very expensive and requires a level of staffing and sophisticated support that would be hard to maintain at 70 geographically distinct institutions. By doing this in our own campus we can also make it available to non-Hughes investigators."

Cech says the imminent publication of the human genome sequence shows that biology is set for a paradigm shift in technological terms. "The amazing thing is that these papers will be published without anything more than a guess of how many genes there are in the genome. It's

somewhere between 30,000 and 100,000 but we don't know because we don't know how to identify a gene unless we've seen it before; we just don't have the tools." He believes the same to be true for proteomics. "How do you evaluate the protein composition of cells when they become transformed—you don't see post-translational modification on a DNA microarray. We need new tools."

The money for the center will come from the Hughes endowment—which currently stands at \$13 billion—and will be diverted from that used to create investigatorships.

Under former director Purnell Chopin, who retired in December 1999, the number of HHMI investigators across the country rose to around 350. But, based on a 5 to 10 year review overseen by

Cech to be published in the coming months, that pool is to be capped. "For the next decade we plan to hold this at 350, for two reasons: first because we think that the impact that we're having is large and if we double again we will not double the impact; secondly, even another 100 scientists would qualitatively change the way we operate. It would be hard to engender the feeling of community that I think we are still able to do at this size."

Cech has also brought a more relaxed style to the organization, according to both observers and his own admission. "We've incorporated the investigators into decision making more than was previously done," he says. "For example, we recently became interested in establishing an HHMI bioethics advisory board, so we invited our investigators to meet with bioethicists and each to explain their needs. The same thing happened when we purchased two synchrotron beam lines for \$8 million at Lawrence National lab at Berkeley—we asked our investigators for advice."

Another change that Cech wants to im-

plement is stopping the pigeon-holing of scientists. He is removing the investigator classifications such as structural biologist, neuroscientist and so forth. "This came to light with computational biology, when we decided that three quarters of our investigators already do this so it doesn't constitute a 'new' HHMI area. We don't want to inhibit anyone from changing fields. What happens is that if a fruit fly scientist was chosen, then organizations presume that's

what we want and nominate their specialists in this area. But we want broad-based researchers with multi-disciplinary approaches to what will have a medical impact downstream."

Always ready with examples to back up his words, Cech mentions Susumu Tonegawa, an HHMI investigator at the



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Institute of Technology, who won the Nobel Prize for discovering immunoglobulin chain rearrangement and who has now phased out immunology research to concentrate on learning and memory research.

Cech's examples are also borne from experience. He was himself an HHMI investigator and won the Nobel Prize in 1989 for discovering the catalysis of biological reactions by RNA molecules, which have come to be known as ribozymes. With the help of Hughes money, he converted his laboratory at the University of Colorado Health Sciences Center, Denver from straight structural biology to X-ray crystallography research.

His appointment as HHMI president marks the first time that a practicing scientist has led this organization. Time will tell whether his post-genomic predictions for a new era in biology come to pass. A summary of Cech's research work can be found at <http://www.hhmi.org/research/investigators/cech.html>.

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