TACKLING ALZHEIMER'S EARLY
Three studies aim to assess the effects of trial drugs on asymptomatic people.

Trial name	Aim	Length	Size	Cost
Alzheimer's Prevention Initiative	To test crenezumab in people who have mutations in the presenilin 1 gene and other genes that cause Alzheimer's in middle age.	5 years	~ 300 people	$100 million
Dominantly Inherited Alzheimer Network	To test three drugs on asymptomatic people with Alzheimer's-linked mutations in genes for presenilins 1 and 2, and amyloid precursor protein.	5 years	160 people	$60 million for 2 years
Anti-amyloid treatment in asymptomatic Alzheimer's disease	To test a drug in asymptomatic people who have high levels of amyloid-β, and some who have a gene variant that increases their risk of Alzheimer's.	3 years	1,000 people	$110 million

compared with a placebo, although this may have been because the drug was administered in lower doses than solanezumab, owing to its higher toxicity. Johnson & Johnson and its partner Pfizer, headquartered in New York city, say that they will vastly scale back development of bapineuzumab.

Increasingly, researchers think that the problem lies not so much with the strategy of targeting amyloid-β as with the timing of treatment. "The major conundrum in the field is: 'are we just treating people too late?'," says Ronald Petersen, director of the Alzheimer's Disease Research Center at the Mayo Clinic in Rochester, Minnesota. Like the fatty plaques in coronary arteries, amyloid-β plaques accrue over a lifetime, says Petersen. And so, just as cholesterol-lowering statins are prescribed for patients in middle age to stave off heart disease in later life, amyloid-blocking drugs given in middle age may prevent Alzheimer's, Petersen says.

But no one knows when amyloid-blocking drugs would need to be taken to prevent the disease, and researchers might have to track tens of thousands of people for decades to determine whether a preventive drug worked. "You can't take every 30-year-old off the street and try a prevention study," says Manji.

Nonetheless, three studies are set to begin by next year that will test whether anti-amyloid drugs can forestall early symptoms of Alzheimer's and arrest cognitive decline in patients who, on the basis of genetic predisposition or amyloid levels, have been identified as being at increased risk of developing the disease (see 'Tackling Alzheimer's early').

The Alzheimer's Prevention Initiative will test crenezumab, a drug developed by Genentech, based in South San Francisco, California, in a large Colombian family that has a rare mutation predisposing members to develop Alzheimer's in middle age. The US$100-million trial will focus on asymptomatic family members for up to five years to see if the drug can stave off their inevitable cognitive decline. The trial will also seek to identify biomarkers, such as amyloid levels from brain scans and in cerebrospinal fluid, that could be used to assess whether crenezumab and other drugs are effective.

"The major conundrum in the field is: 'are we just treating people too late?'."

"We need to launch a new era in Alzheimer's-prevention research to set the stage to rapidly evaluate treatments," says Eric Reiman, executive director of Banner Alzheimer's Institute in Phoenix, Arizona, who is co-leading the Colombia trial. With such markers identified, drug companies could quickly get a sense of whether or not a drug is preventing Alzheimer's, saving precious money and time, he says.

Drug agencies, including the US Food and Drug Administration and the European Medicines Agency, are keeping a close watch on those efforts. In theory, approval for preventive drugs could be assessed on the basis of clinical trials measuring changes in biomarkers, or surrogates, instead of traditional measures of cognitive improvement. However, regulatory agencies are likely to set a very high bar for what constitutes a proven surrogate, says Siemers.

Reiman's study is already bankrolled. But the two other imminent trials — one led by the Alzheimer's Disease Cooperative Study, a US government-funded programme, and the other by researchers at Washington University School of Medicine in St Louis, Missouri — are still looking for money. Many Alzheimer's experts hope that this summer's bleak news will not scare off investors.

"We've had this concern for quite some time," says Reiman, "that if these trials were negative we would see some major stakeholders and investors abandon amyloid-modifying treatments. We think that would be throwing the baby out with the bath water, and abandoning Alzheimer's disease." ■

CONSERVATION

India's forest area in doubt

Reliance on satellite data blamed for over-optimistic estimates of forest cover.

BY NATASHA GILBERT

To judge from India's official surveys, the protection of its forests is a success. Somehow, this resource-hungry country of 1.2 billion people is managing to preserve its rich forests almost intact in the face of growing demands for timber and agricultural land.

But a senior official responsible for assessing the health of the nation's forests says that recent surveys have overestimated the extent of the remaining forests. Ranjit Gill of the Forest Survey of India (FSI) claims that illegal felling of valuable teak and sal trees has devastated supposedly protected forests in the northeast of the country. He and other experts also say that an over-reliance on inadequate imaging by an Indian satellite system is making such destruction easy to overlook.

In February, the FSI, part of the government's Ministry of Environment and Forests, released the *India State of Forest Report 2011*. This biennial survey used images from India's remote-sensing satellite system and estimated that forest covered 692,027 square kilometres of the country — roughly 23% of India's land area — a decline of just 367 km^2 on the tally reported in 2009, and a much smaller loss than in Brazil, for example, where more than 13,000 km^2 of forest was cleared over the same period. But Gill, a joint director of the FSI, is openly critical of the FSI's assessment.

"We have to accept the grave reality that the current figure of forest cover in India is way over the top and based on facile assumptions," Gill argues. To bring these allegations to light,

he has mounted a legal case for consideration by India's Central Empowered Committee (CEC), a panel of experts appointed by the nation's Supreme Court to rule on issues concerning forests and wildlife.

Gill alleges that the government of Meghalaya state in northeast India has failed to act sufficiently on evidence that illegal felling and coal mining is ravaging the region's protected forests. He says that he has seen the deforested areas at first-hand, and reported them to the state government (see 'On the stump'). He is also concerned that the 2011 forest report records large areas in Meghalaya as open or dense forest, when he believes that much of the land had been cleared and then allowed to regrow saplings or bamboo.

On a field survey last year, Gill and three FSI colleagues saw that parts of the Dibru Hills protected forest in Meghalaya had been illegally felled. He confirmed his field observations with 2006 data from the LANDSAT Earth-observing satellites operated by NASA and the US Geological Survey. The satellite data showed that roughly 150,000 trees in the area had been cut down in the preceding years, across an area of about 10 km^2.

Gill also points to an investigation in 2006 by Meghalaya state's forest and environment department. The report, which he obtained through a freedom-of-information request and showed to *Nature*, found illegal saw mills operating in the area, as well as freshly felled logs. The region has "come under tremendous pressure and suffered serious depletion, which has reached alarming proportions", that report says.

According to documents submitted to the CEC, the Meghalaya state government claims that only 670 trees were felled in the Dibru Hills forest from 2004 to 2007. In Gill's view, "the records and reports of the government of Meghalaya are not a true picture of the positions on the ground". P. B. O. Warjri, chief secretary of the government of Meghalaya, told *Nature* that Gill's claims are "not true".

But another state government report obtained by Gill documents similar illegal deforestation in the nearby Rongrenggre protected forest, where 60–70% of the tree cover has been lost. The report also found evidence that local forest rangers were involved in the illegal timber trade, and that illegal coal mining in the area was taking place in "full knowledge" of the rangers. Gill is concerned that similar lapses are happening, and not being reported, in other parts of the country.

Other tropical-forest researchers share Gill's fears about India's forests. "The ongoing loss and attrition of native forest in India is quite widespread, although it isn't being captured by the government's satellite data on forest cover," says William Laurance, a conservation biologist at James Cook University in Cairns, Queensland, Australia. "Much of this forest disruption is illegal, and encroachment into protected areas and reserves is not uncommon, in my experience."

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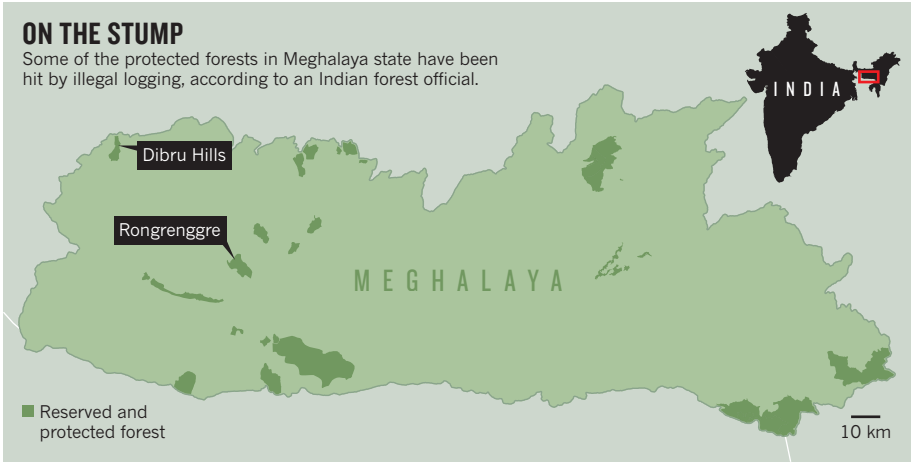

FOREST & ENVIRON. DEPT, MEGHALAYA

RANJIT SINGH GILL

Forest officer Ranjit Gill says that he has evidence of widespread deforestation in Meghalaya (above).

Anil Kumar Wahal, the director of the FSI, denies that forest cover has been overestimated. The FSI team that conducted the field visit in May 2011, of which Gill was part, "reported a few sporadic patches of felling, and old stumps in the field, but nothing as glaring as felling of vast swathes of forest", he says. But Wahal admits that the "selective" cutting of trees "would not register in the satellite imagery due to the technological limitation of the medium-resolution sensor used for the purpose of forest-cover mapping".

Gill notes that the instrument, which flies on an Indian remote-sensing satellite, produces images with a resolution of 23.5 metres per pixel, too coarse to unequivocally identify small-scale deforestation. Instead, he says, the forest survey should use a newer instrument, already operating on an Indian satellite, that provides a resolution of 5.8 metres per pixel.

The FSI uses the lower-resolution instrument for its national survey because it offers continuous coverage of very large areas, explains Wahal. "Gap-free data are really essential," he says. "Using high-resolution data would also entail much more manpower and time, so a balance has to be struck." The FSI is, however, using the higher-resolution instrument for some small-scale surveys, he adds.

Gill argues that the FSI still needs to conduct more on-the-ground surveys to corroborate its satellite estimates of forest cover. Without this reality check, it can be difficult to tell the difference between native forests and, for example, bamboo. He is calling on the CEC to order a visit to the forests to investigate the extent of the destruction. A verdict is expected from the CEC by the end of the year.

Last year, India's government grabbed headlines with a US$10-billion, decade-long plan — the National Mission for a Green India — to create or improve 10 million hectares of forest. But if Gill is right, it faces a more urgent task: to chart and protect the forests that remain. ■