Medical Xpress

Scientists map imprinted genes in human genome

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Cover, Genome Research. Credit: Genome Research

Scientists at Duke University have created the first map of imprinted genes throughout the human genome, and they say a modern-day Rosetta stone – a form of artificial intelligence called machine learning – was the key to their success.

The study revealed four times as many imprinted genes as had been previously identified and is featured on the cover of the December 3 issue of *Genome Research*.

In classic genetics, children inherit two copies of a gene, one from each parent, and both actively shape how the child develops. But in imprinting, one of those copies is turned off by molecular instructions coming from either the mother or the father. This process of "imprinting" information on a gene is believed to happen during the formation of an egg or sperm, and it means that a child will inherit only one working copy of that gene. That's why imprinted genes are so vulnerable to environmental pressures: If the only functioning copy is damaged or lost, there's no backup to jump in and help out.

Many of the newly-identified imprinted genes lie within genomic regions linked to the development of major diseases like cancer, diabetes, autism, and obesity. Researchers say that if some of these genes are later shown to be active in these disorders, they may offer clues to better disease prevention or management.

"Imprinted genes have always been something of a mystery, partly because they don't follow the conventional rules of inheritance," says Dr. Randy Jirtle, a genetics researcher in the departments of radiation oncology and pathology at Duke and a senior author of the study. "We're hoping this new roadmap will help us and others find more information about how these genes affect our health and well-being."

The technical wizardry needed to find the genes fell to Dr. Alexander Hartemink, the other senior author of the study and an assistant professor in Duke's department of computer science, and Philippe Luedi, the first author of the study. They fed sequence data from two types of genes – ones known to be imprinted and ones believed not to be imprinted – into a computer and asked it to discover the differences. This machine learning approach led to an algorithm, which was able – like the original Rosetta stone – to decode seemingly impenetrable data, in this case, specific DNA sequences that pointed to the presence of imprinted genes.

“We can’t say for certain that we identified all of them, but we think we found a large number,” says Hartemink.

Jirtle, who has studied imprinting for years, notes that imprinting is an epigenetic event, meaning it’s something that can change a gene’s function without altering the sequence of its DNA. “Imprinted genes are unusually vulnerable to pressures in our environment – even what we eat, drink, and breathe. On top of that, epigenetic changes can be inherited. I don’t think people realize that.”

Several years ago, Jirtle showed that Agouti mice – normally fat and yellow – when fed certain dietary supplements, would produce brown, normal weight babies. The babies’ Agouti genes, the ones responsible for color, were the same as the mother’s, yet they looked different. “That’s epigenetics in action,” says Jirtle.

It’s estimated that imprinted genes comprise about 1 percent of the human genome, and until now, only several dozen had been identified. Using their new “Rosetta stone”, however, Jirtle and Hartemink found 156 new likely imprinted genes, and validated two particularly interesting ones on chromosome 8, where none had been found before. One of them, KCNK9, is mostly active in the brain, is known to cause cancer, and may also be linked to bipolar disorder and epilepsy. The second, DLGAP2, is a possible bladder cancer tumor suppressor gene.

Hartemink says experiments to confirm that all 156 new genes are truly imprinted – and not just statistically likely candidates – will be difficult, mostly because gene expression varies from tissue to tissue and most genes turn on and off over time. “We’ve certainly narrowed the field, but we have a whole lot of work ahead of us.”

Source: Duke University Medical Center