'Junk' DNA now looks like powerful regulator, researcher finds

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Large swaths of garbled human DNA once dismissed as junk appear to contain some valuable sections, according to a new study by researchers at the Stanford University School of Medicine and the University of California-Santa Cruz. The scientists propose that this redeemed DNA plays a role in controlling when genes turn on and off.

Gill Bejerano, PhD, assistant professor of developmental biology and of computer science at Stanford, found more than 10,000 nearly identical genetic snippets dotting the human chromosomes. Many of those snippets were located in gene-free chromosomal expanses once described by geneticists as "gene deserts." These sections are, in fact, so clogged with useful DNA bits - including the ones Bejerano and his colleagues describe - that they've been renamed "regulatory jungles."

"It's funny how quickly the field is now evolving," Bejerano said. His work picking out these snippets and describing why they might exist will be published in the April 23 advance online issue of the *Proceedings of the National Academy of Sciences*.

It turns out that most of the segments described in the research paper cluster near genes that play a carefully orchestrated role during an animal's first few weeks after conception. Bejerano and his colleagues think that these sequences help in the intricate choreography of when and where those genes flip on as the animal lays out its body plan. In particular, the group found the sequences to be especially abundant near genes that help cells stick together. These genes play a crucial role early

in an animal's life, helping cells migrate to the correct location or form into organs and tissues of the correct shape.

The 10,402 sequences studied by Bejerano, along with David Haussler, PhD, professor of biomolecular engineering at UC-Santa Cruz, are remnants of unusual DNA pieces called transposons that duplicate themselves and hop around the genome. "We used to think they were mostly messing things up. Here is a case where they are actually useful," Bejerano said.

He suspects that when a transposon is plopped down in a region where it wasn't needed, it slowly accumulated mutations until it no longer resembled its original sequence. The genome is littered with these decaying transposons. When a transposon dropped into a location where it was useful, however, it held on to much of the original sequence, making it possible for Bejerano to pick out.

In past work, Bejerano and his co-workers had identified a handful of transposons that seemed to regulate nearby genes. However, it wasn't clear how common the phenomenon might be. "Now we've shown that transposons may be a major vehicle for evolutionary novelty," he said.

The paper's first author, Craig Lowe, a graduate student in Haussler's lab at UC-Santa Cruz, said finding the transposons was just the first step. "Now we are trying to nail down exactly what the elements are doing," he said.

Bejerano's work wouldn't have been possible without two things that became available over the past few years: the complete gene sequence of many vertebrate species, and fast computers running sophisticated new genetic analysis software. "Right now it's like being a kid in a candy warehouse," Bejerano said. Computer-savvy biologists have the tools to ask questions about how genes and chromosomes evolve and change,

questions that just a few years ago were unanswerable.

Bejerano and his colleagues aren't the first to suggest that transposons play a role in regulating nearby genes. In fact, Nobel laureate Barbara McClintock, PhD, who first discovered transposons, proposed in 1956 that they could help determine the timing for when nearby genes turn on and off.

Source: Stanford University Medical Center