original dac that, over time, evolved into an entirely new function and way of unique way of walking about for spiders.

“Species constantly adapt and evolve by inventing new body features,” said Prpic. “Our work shows how a gene can be duplicated and then used during evolution to invent a new morphological feature.”

**Reference**


Joseph Caspermeyer*1

1MBE Press Office

*Corresponding author: E-mail: MBEpress@gmail.com.

doi:10.1093/molbev/msv232

Advance Access publication November 24, 2015

---

**A Dominant Evolutionary Theme Emerges to Better Predict Clinical Outcomes for Cancer**

Despite the decades long battle since the “war on cancer” was first declared, major breakthroughs toward improving clinical outcomes have remained elusive. Now, with advanced sequencing, scientists have increasingly entered the fray from an evolutionary perspective toward cancer in the hopes of gaining new insights.

Chen and He (2016) have used a new computational approach to show that as tumors evolve, no matter what the tissue or cell type, a dominant theme has emerged. Those that are trending toward a more primitive, or embryonic stem cell (ESC) state—have a worse clinical outcome.

The authors applied their systems biology approach to study global gene expression profiles from 107 cells types, and in more than 3,000 tumors representing 18 different types of solid tumor cancers. The authors performed their analysis and showed that, regardless of the origins of the tissue, this common and robust pattern emerged. Like in ancient times, where despite the distance, all roads led to Rome, they showed that the distance to the ESC state may represent a robust and predictive measurement for various types of cancer. This is in line with a cancer evolution model recently demonstrated by the same group that cancer is a reverse evolutionary process back to the unicellular “ground state” by erasing multicellularity-associated cellular features.

“The essence of Darwin’s theory is that evolution is driven by purposeless mutations that are subsequently selected by environments, so there is often no predefined destination in organismal evolution,” said He. “In this study, we showed that, distinct from organismal evolution, cancers of various types evolve toward a predefined cellular destination, a finding with implications to both evolutionary biology and cancer prognosis.”

For cancer evolution, regardless of the environment, the predefined final destination is the ESC state, and the closer the evolutionary distance, the poorer the prognosis.

**Reference**


Joseph Caspermeyer*1

1MBE Press Office

*Corresponding author: E-mail: MBEpress@gmail.com.

doi:10.1093/molbev/msv233

Advance Access publication November 20, 2015

---

**Predicting the Human Genome Using Evolution**

To gain a clearer picture of health and disease, scientists have now provided an independent reference for all human variation by looking through the evolutionary lens of our nearest relatives. Such a powerful approach has been developed by Temple University professor Liu et al. (2016) and was detailed in the advanced online publication of *Molecular Biology and Evolution*.

“There are two ways to generate a map of the human genome variation: one is to get genomes of all the humans and build a compilation as the 1000 Genomes Project and others have undertaken,” said Kumar, a Temple University professor and director of the Institute for Genomics and Evolutionary Medicine (iGEM). “The alternative, which is the basis of our approach, is to compile all genome data
from other species and predict what the human sequence reference should be.”

By observing evolution’s “greatest hits” (and misses) and the history of the major themes and patterns of genome conservation (and divergence) across many species, Kumar’s approach predicts probable mutations that will be found among people and the fate of human variation.

His research team relied on an evolutionary tree that included 46 vertebrate species spanning over 500 My of life on Earth to predict the evolutionary probability (EP) of each possibility at each position of our genome. They applied their new method on all protein-coding genes in the human genome (more than 10 million positions). Consistent with the knowledge that most mutations are harmful, they found very low EPs (lower than 0.05) for a vast majority of potential mutations (94.4%).

Next, they produced a complete evolutionary catalog of all human protein variation, or evolutionary variome (eVar), that can be used to better understand human diseases and adaptations. And, it can be directly applied to the genomes of any other species. Their eVar was also compared against available human sequence data from the 1000 Genomes Project to look at benign and disease mutations, and found that the use of EPs could correctly diagnose them. They also used a cancer benchmark data set to show that EPs accurately predicted cancer-related mutations.

Finally, they found a large number (36,691) of variations, that according to the EP data were evolutionarily improbable (EP < 0.05), but were found 100% of the time in the 1000 Genomes Project data—which Kumar suggests could be strong candidates for adaptive evolution—and what may make us uniquely human.

“The fascinating part of the story is that once we know what our ancient evolutionary history predicts our sequence to be, then we can compare this expectation to what we observe in human populations today. When there is a discordance such that an unlikely variant is found in many people, it directly indicates that something has changed about us or the protein,” said Kumar.

Reference

Joseph Caspermeyer* 1
1MBE Press Office
*Corresponding author: E-mail: MBEpress@gmail.com.
doi:10.1093/molbev/msv257