Repurposing genetics to search for ‘healthy’ genes

For most us, the scientific promise associated with understanding the human genome exists in uneasy tension with the quiet terror with which we regard the demons we might discover lurking within our own DNA.

Our abiding unease makes sense, given the way genetics has entered our consciousness – typically something along the lines of, “Your genes hold something bad; knowing this danger may help you mitigate the risk.”

Contemporary use of genetics in oncology (think Foundation Medicine) falls squarely into this category. So does carrier screening of couples (think Counsyl); experts suggest that about 30 percent of us – MGH/Broad Institute geneticist Daniel MacArthur believes the figure may be as high as 50 percent — carry a recessive copy of at least one lethal genetic mutation – a mutation that would prove fatal if inherited from each parent.

Yet, there’s another approach to genetics that’s recently gaining traction, a methodology that seems to look at the genome through a more hopeful and positive lens. In this “happy genetics,” the goal is to find people who are unexpectedly healthy, and then search for the genes potentially responsible.

One example of this is the Resilience Project, an effort (led by Eric Schadt of the Icahn School of Medicine and Stephen Friend of Sage Bionetworks) that specifically tries to identify people who should be sick, but aren’t. Investigators are screening healthy people and looking for examples of someone who carries a known mutation that should result in serious childhood disease, yet who is healthy. The hope is to identify what’s known as “suppressors” – genetic variations in a second gene that offsets a problem with the first gene. Such suppressor analysis is a tool from classic genetics that can reveal unexpected biological relationships and define novel physiological pathways. It can also point to potential therapeutics – a product that mimics the biological activity of the suppressor.

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