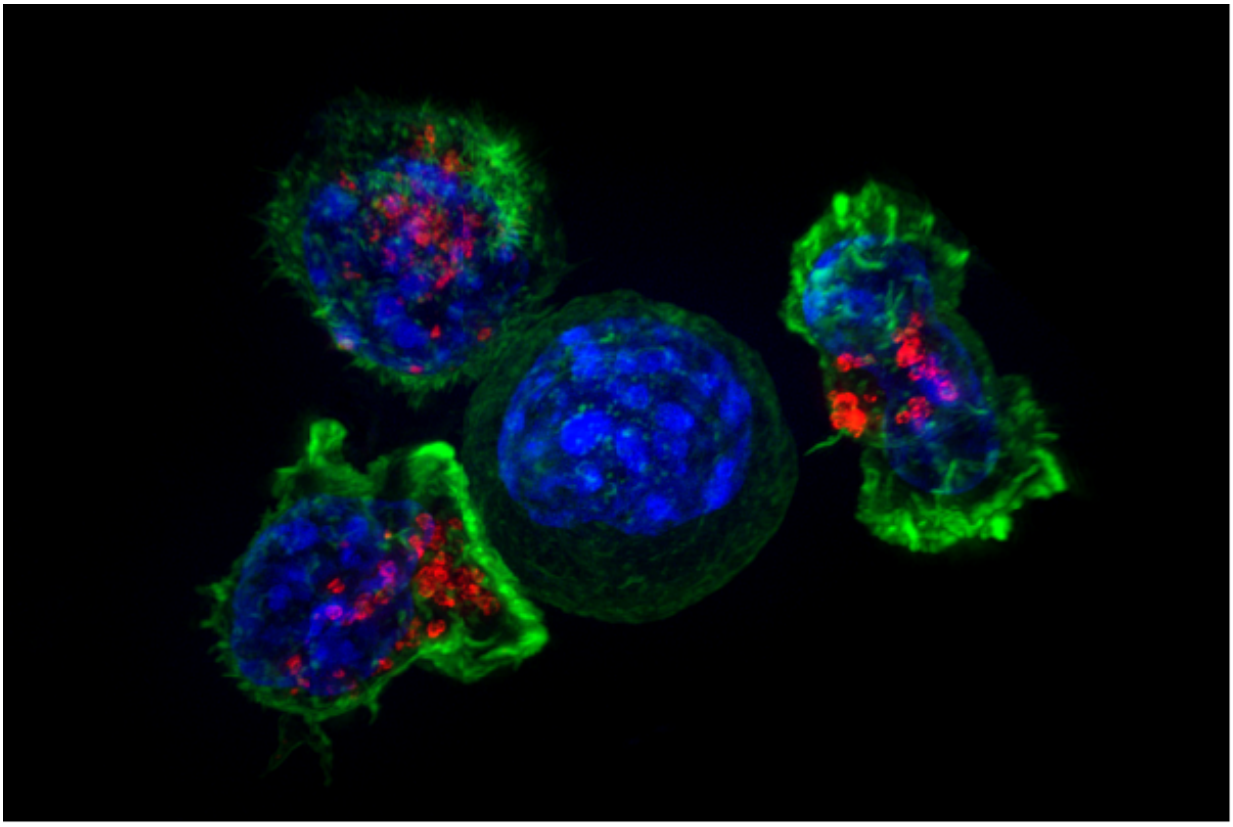
MedicalXpress

Study discovers link between cancer and autism

April 13 2016



Killer T cells surround a cancer cell. Credit: NIH

A group of University of Iowa researchers has shown that although patients who have been diagnosed with an autism spectrum disorder (ASD) have a higher burden of mutations in cancer-promoting

oncogenes, they actually have lower rates of cancer.

The multidisciplinary team, led by Benjamin Darbro, MD, PhD, assistant professor of medical genetics in the Stead Family Department of Pediatrics at the UI Carver College of Medicine, analyzed large, publicly available genomic databases of patients with autism and found that, compared to a control set , autistic patients have significantly higher rates of DNA variation in oncogenes. The team followed up this result with an analysis of the University of Iowa Hospitals and Clinics' electronic medical record (EMR) and discovered that patients with a diagnosis of autism are also significantly less likely to have a co-occurring diagnosis of cancer.

"It's a very provocative result that makes sense on one level and is extremely perplexing on another," Darbro says.

The study was published recently in the journal *PLOS ONE.*

Darbro and his team used exome sequencing data from the ARRA Autism Sequencing Collaboration and compared that data to a control cohort from the Exome Variant Server database. They found that rare, coding variants within oncogenes were greatly enriched in the ARRA ASD cohort. By comparison, variants were not significantly enriched in tumor suppressor genes.

To ensure that the genetic differences were not simply technical artifacts but actually bona fide differences in genetic architecture in autism, the researchers ran numerous controls. As expected, they found that individuals with autism had many more DNA variations in genes previously associated with autism, epilepsy, and intellectual disability compared to control individuals. There was no difference between the autism and control groups when they examined genes involved in other, unrelated conditions such as skeletal dysplasia, retinitis pigmentosa,

dilated cardiomyopathy, and non-syndromic hearing loss.

They then turned their attention to the EMR at UI Hospitals and Clinics and conducted a retrospective case-control analysis comparing 1,837 patients with autism spectrum disorder to 9,336 patients with any other diagnosis, and determined what proportion of each group of patients carried a cancer diagnosis. They found that for children and adults with ASD there appeared to be a protective effect against cancer; 1.3 percent of patients with ASD also had a diagnosis of cancer compared to 3.9 percent of the control patients. However, the protective effect was strongest for the youngest group of patients and decreased with age.

For those individuals with autism who were under 14 years of age, the odds of having cancer were reduced by 94 percent compared to individuals in the same age range without autism. Both males and females with ASD demonstrated the protective effect.

When the research team determined the rates of other systemic diseases besides cancer in the autistic population, such as high blood pressure and diabetes, they found no relationship. Furthermore, unlike what they found for autism, they found no relationship with cancer when they examined the rates of other common conditions such as heartburn (esophageal reflux), allergies (allergic rhinitis), eczema (atopic dermatitis), and short stature. This demonstrated that the inverse relationship observed between autism and cancer is not due to a technical artifact.

Autism spectrum disorder is a general term for a group of disorders that affect brain development. Autism is characterized by impaired social interaction, verbal and nonverbal communication skills, and repetitive behaviors. As Darbro points out, autism is also one symptom of many inherited cancer syndromes caused by mutations in a single gene. In fact, several genes implicated in causing hereditary tumor syndromes overlap

with those involved in syndromic causes of neurodevelopmental disorders such as autism.

"The overlap in genes between those known to promote cancer and those implicated in syndromic neurodevelopmental disorders is not new, but what we've shown is that this overlap is much broader at the genetic level than previously known and that somehow it may translate into a lower risk of cancer," Darbro says.

Researchers also ran their datasets through stringent control analyses, examining the autism cohort for differences in genes associated with diseases other than cancer. They found that while patients with autism showed enrichment of variation in genes linked with autism (epilepsy and intellectual disability) they were not enriched for variation in genes linked to unrelated disorders including retinitis pigmentosa, dilated cardiomyopathy, and non-syndromic hearing loss. These genetic controls demonstrate that the team's findings are not simply technical artifacts of differences in sequencing coverage, but reflect the genetic architecture of an autism cohort.

The findings raise questions that might have implications for new ways of treating both cancer and ASD. For example, could the genetic variants that seem to provide protection against cancer in people with ASD, be exploited to develop new anti-cancer treatments? Or could current cancer drugs that target the genetic pathways found to overlap with ASD also be useful for treating ASD? This last question is already being pursued by other scientists in clinical trials testing the potential benefits of anti-cancer drug for autism patients.

More information: Benjamin W. Darbro et al. Autism Linked to Increased Oncogene Mutations but Decreased Cancer Rate, *PLOS ONE* (2016). DOI: 10.1371/journal.pone.0149041

Provided by University of Iowa