

## Cancer genetics may aid diagnostics of developmental disorders

*De novo* mutations are a major contributor to developmental disorders (DDs) such as autism and intellectual disability. Advances in sequencing technologies have enabled the identification of up to 200 candidate genes that can harbor DD causing mutations. However, it remains challenging to discover true causal genes and variants amongst the many genetic changes detected by sequencing studies. In this issue, Qi et al (*Hum Mutat* x: y-z, 2016) demonstrate the feasibility of utilizing the more abundant and better annotated cancer genome data in the hopes of more rapidly annotating these debilitating *de novo* mutations to improve diagnostics and gain a better understanding of the underlying etiology.

Neurodevelopmental disorders (NDDs) and cancer share a strong genetic component in their etiology, and overlapping genetic architecture. For example, inherited point mutations in the tumor suppressor gene *NF1* not only cause tumor phenotypes - neurofibromatosis - but also cognitive and learning disability (Jett et al., *Genet Med* 12: 1-11, 2010). It is well-known that somatic mutations in *NF1* and other tumor suppressor genes and proto-oncogenes (cancer driver genes) can induce cancer formation. In this issue, Qi et al. demonstrate that germline damaging *de novo* variants found in DD patients (primarily NDDs) are significantly enriched in cancer driver genes compared to non-driver genes. Qi et al. estimate that one third of the DD genes are cancer driver genes. They go on to show that in DD patients, oncogenes were significantly enriched for missense *de novo* mutations predicted to be damaging. This suggests a similar mode of action (aberrant activation) in both cancer and DD, at least for some mutations.

Given the apparent deep genetic connection between cancer and developmental disorders, it does beg the question whether individuals with developmental disorders have an increased cancer risk. Although conflicting reports exist, most studies support an increased cancer incidence in autism spectrum disorder (ASD) patients over age-matched controls (Chiang et al., *J Pediatr* 166: 418-23, 2015). Intriguingly, in other NDDs such as schizophrenia, decreased cancer risk has been noted (Tabares-Seisdedos and Rubinstein, *Nat Rev Neurosci* 14: 293-304, 2013). It would be illuminating to test whether the degree of functional concordance of mutations in cancer genes mirrors these contrasting associations. If so, the discovery of shared pro- or anti-proliferative pathways might motivate drug repurposing efforts, such as the ongoing clinical trials of everolimus in autism or the anti-psychotic thioridazine in acute myeloid leukemia.

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