20th World Congress on
PEDIATRICS AND ADOLESCENT MEDICINE
&
20th World Congress on
PEDIATRIC ONCOLOGY AND NURSING
September 17-18, 2018 | Philadelphia, USA

Sharon J Diskin

Children's Hospital of Philadelphia, USA

The genetic basis of neuroblastoma predisposition

Neuroblastoma is a malignancy of the developing sympathetic nervous system which accounts for 12% of childhood cancer deaths. Appoximately 1-2% of cases are inherited in an autosomal dominant fashion and mutations in ALK and PHOX2B have been identified as the major drivers of this subset. Here, we report on efforts to identify the genetic basis of sporadic neuroblastoma (98% of cases) using a combination of genome-wide association studies (GWAS) and next generation sequencing. To date, we have genotyped 6,201 neuroblastoma cases and 32,240 healthy controls for GWAS and performed whole-genome or whole-exome sequencing (WGS or WXS) on matched tumor-normal DNA pairs from 776 cases to identify rare germline mutations. GWAS efforts have led to the publication of over a dozen susceptibility loci and the identification of genes influencing both tumor initiation and progression. We have now performed a large multi-ethnic GWAS combining cohorts of European ancestry, African American and Hispanic populations. We identified eleven new susceptibility loci ($P < 5.0 \times 10^{-8}$) and discovered a rare 550-kb deletion on chromosome 16p11.2 enriched in cases vs. controls (Odds Ratio: 15.4; 95% C.I. 4.1-57.9). From sequencing studies, we observed enrichment of truncating BARD1 mutations in neuroblastoma cases (1.2%, $p<0.001$) and estimate that ~10% of children with neuroblastoma harbor a rare pathogenic germline mutation in a known cancer predisposition gene. Collectively, these studies are defining the landscape of genetic predisposition in neuroblastoma. Ongoing efforts are focused on identifying the functional significance of rare germline mutations and translating these findings to the clinic.

Biography

Sharon Diskin completed her PhD in 2008 from the University of Pennsylvania and postdoctoral studies at The Children's Hospital of Philadelphia in 2012. She is an Assistant Professor of Pediatrics at the University of Pennsylvania and Children's Hospital of Philadelphia. Her research program is focused on identifying the genetic basis of childhood cancers, including the complex interplay between germline and tumor genomics. She has published more than 47 papers in reputed journals and serves as a reviewer or editorial board member of multiple journals.

diskin@email.chop.edu

Notes: