Interactions between germline and tumor genomes

Abstract: This presentation will provide an overview of the ways in which the germline genome can shape the somatic mutational landscape in tumors. Emerging data from our lab and others that will be highlighted in this talk suggest that germline genetic variants impact somatic events in tumors. Pathogenic germline variants in high-risk genes such as BRCA1 and BRCA2 impact the types of observed mutations in tumors. Mouse models show strain-specific losses and gains in tumors suggesting that modifier risk alleles can influence which copy number changes are selected during tumor development. Tumor sequencing data have revealed significant differences in mutation frequencies between racial and ethnic groups. Some of these differences can be attributed to environmental exposure, such as smoking frequency, but disparities persist even after adjustment for known factors. Well-described examples include TP53 mutations that are seen at elevated rates in breast cancers in African-Americans compared to Asian and non-Hispanic White women. Results from discovery genome-wide association studies to identify germline variants that associate with somatic TP53 and PIK3CA mutations in breast tumors will be discussed. Data from these studies support the role of the germline genome in selection of somatic events during tumor development.

About the Speaker: Amanda Ewart Toland, PhD, FACMG, is a Professor and Vice Chair of the Department of Cancer Biology Genetics with a joint appointment in the Division of Human Genetics, Department of Internal Medicine at the Ohio State University (OSU). She is also co-Director of the OSU Comprehensive Cancer Center Genomics Shared Resource. She received her PhD in Human Genetics from the University and is Board Certified by the American College of Medical Genetics and Genomics in PhD Medical Genetics. She did her clinical training in genetics at the University of California San Francisco followed by a research postdoctoral fellowship in the laboratory of Allan Balmain. Her laboratory studies the role of genetic variants in modifying disease risk of hereditary and sporadic cancers using a variety of in vitro, in vivo and population-based approaches.