A090 · Identifying Germline Drivers of Neuroblastoma by Their Interaction with Somatic Mutation

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Session: Day 1 · Thu Oct 1, 2026 · 2:15–4:15 PM

Neuroblastoma is a pediatric cancer that occurs in infancy, with an average age of onset being 17-18 months. Due to the early onset of the cancer, its development is likely influenced by germline variants.But, because the cancer is rare, it is hard to identify associated variants. To identify relevant variants, we hypothesize that instead of relying only on how frequently they occur, we can also identify if they are associated with particular somatic mutations. To investigate this hypothesis, we analyze data from the Kids First Neuroblastoma project, which profiles germline genetic variation and matched somatic mutations for over 200 children with neuroblastoma. We compile gene-based burden of rare germline variants, and for each burdened gene, we assess whether its mutation is associated with any recurrent copy number changes, single nucleotide mutations, or structural mutations. After identifying associated pairs of germline and somatic mutations, we aim to assess if this approach distinguishes clinically meaningful subgroups of patients. To this end, we test whether patients bearing both a germline and significantly associated somatic mutation have distinct survival outcomes; a different age of onset; or a distinct tumor location.

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