

**Figure S7**. Decision tree for assessing disease relevance of germline variants. Germline P/LP variants were evaluated in the context of each patient's tumor type to determine potential relevance. We considered a germline variant relevant to disease if the gene had a known association with the child's tumor type (a), or if there was specific molecular evidence supporting a functional consequence of the mutation in the tumor (b). If neither of these criteria were met, the relevance of the variant in the disease was considered to be unknown. Tumor molecular evidence included loss of the wildtype gene copy through focal LOH, presence of hypermutation or specific mutation signatures; or aberrant gene expression resulting from splicing defects or allele specific expression.