

TARGET Neuroblastoma Models

TARGET also produced the following models, generated in the lab of Dr. Patrick Reynolds, Texas Tech University Health Sciences Center. They all have EBV Immortalized Normal samples.

TARGET Neuroblastoma Cell Line and Patient-Derived Xenograft Models

Case	Samples	Description
TARGET-30-NAABZJ	- primary tumor - cell line from primary tumor at diagnosis - cell line from bone marrow at progression	The pretreatment primary tumor consists of a single dominant clone that shares many mutations with the matched pretreatment cell line. Fewer mutations are shared with a cell line established upon progression. The single subclone present in the primary tumor is not evident in the derivative cell line. However, the cell line has acquired an additional subclonal population well supported by 75 mutations that are not evident in the match primary nor is there evidence of this clone in the cell line established upon progression. Therefore, this subclone may have arisen in culture or have been an undetected low frequency subclone in the primary that was sensitivity to treatment.
TARGET-30-NAABZK	- cell line from primary tumor at diagnosis - cell line from pleural fluid at diagnosis - cell line from bone marrow after induction chemo	Cell lines from the same pretreatment tumor (tissue and effusion) share many mutations and a common subclone (61% cancer cell fraction). The cell line from the matched posttreatment tumor has a dramatic increase in somatic mutation burden, although many of these are found in subclonal populations; one related to the shared pretreatment (160/162 shared) and a second completely unique to the posttreatment case.
TARGET-30-NAABZM	- cell line from bone marrow at diagnosis - cell line from bone marrow at progression	Cell lines established before and after treatment share a common core set of somatic mutations shared across clonal and subclonal populations. However, each of these populations have hundreds of

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	(heavily treated with chemo)	additional unique mutations, suggesting significant divergence and possible selection of subclonal populations coexisting at similar cancer cell fractions in each cell line. Based on our current data, we cannot verify whether two subclonal populations coexist in each line without further analysis (e.g., via single-cell sequencing).
TARGET-30-NAABZN	- cell line, postmortem blood heavily treated with chemo - mouse xenograft postmortem blood sample	Cell line and mouse xenograft derived from the same postmortem blood sample share a majority of mutation patterns, although the mouse xenograft lacks the higher frequency subclones found in the cell line. Possibly, the subclone at 20% cancer cell fraction in the cell line contained additional mutations that conferred a growth advantage over higher frequency population lacking the 41 additional mutations in these clones. Further genetic divergence is evident from additional singleton mutations at very low allele fractions (<1%) in each case, though these require verification by orthogonal methods.
TARGET-30-PAMYEF	- cell line from postmortem blood, room air - cell line from postmortem blood, 5% O₂ - xenograft from postmortem blood	Cell lines derived from the same primary share a large fraction of mutations, although each contains hundreds of mutations unique to the growth conditions. In TARGET-LEFT, the cell line grown under hypoxic conditions contains a greater number of mutations (956 versus 910) as well as an additional subclone supported by 6 mutations. The higher-level subclonal structure is consistent with a mouse xenograft derived from the same material. The mouse xenograft has incurred additional subclones, albeit with fairly weak mutational support. This pattern is reversed in TARGET-RIGHT whereby the

Case	Samples	Description
		hypoxic cell line has fewer mutations (928 versus 1005) and no low frequency subclone. The subclone in the mouse xenograft appears to be derived from a subclone common across all model organisms, although the lower cancer cell fraction suggests it is not well suited to growth in the xenograft or may have been outcompeted for growth by the clonal population.
TARGET-30-PASXWX	- cell line from postmortem blood - postmortem blood cell line, 5% O₂ - xenograft of postmortem blood cell line	