TARGETING FUSION-DRIVEN SARCOMAS

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Dr. Khan anticipates the publication of manuscripts and similar communications in appropriate scientific peer-reviewed journals that support open-access sharing of data.

FINAL REPORT SUMMARY

Several aggressive childhood malignancies depend on the function of molecules that contain parts of two different proteins, often referred to as fusion proteins. Strategies aimed at the inactivation of such cancer-associated fusion proteins have resulted in several clinical success stories. For example, the inhibition of the activity of a fusion protein as in sarcomas with NTRK fusions. Importantly, we think recent tech-nological advances that allow the investigation of every human gene or thousands of compounds will help the development of similar approaches to treat other fusion protein-driven cancers. However, to make full use of these new large-scale genetic or drug screening approaches, we need to develop many critical resources.

The goal of this initiative is the generation of panels of modified cell lines from two fusion-driven sarcomas: Ewing sarcoma (EWS) and alveolar rhabdomyosarcoma (ARMS). The proposed modifications will enable researchers to measure the amount of the fusion protein present in a sarcoma cell or purify more effectively each fusion protein and the other proteins they bind. Over phase 1 of this research initiative, we have successfully made strides into generating fusion gene tagged of at least one EWS and one ARMS cell line.

"To achieve our goal, we are using CRISPR-based gene editing to insert a reporter gene or tag into the genome of EWS or ARMS cell lines in-frame with the fusion oncogene. These lines will be invaluable resources for addressing goals proposed as part of future ALSF-funded projects and for the broader pediatric oncology community."

FUTURE PLANS

The next phase of our work will focus on establishing the remaining cell lines and validating and characterizing these cell line resources with the transfer of these resources to the research community for their use in fueling the next phase of discovery efforts focused on these difficult to treat pediatric cancers.