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Mutated FGFR4 protein helps a childhood cancer spread

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Rhabdomyosarcoma (RMS) is a childhood cancer thought to originate from skeletal muscle. In patients whose disease has spread (metastasized) from the initial tumor site the chance of long-term survival is poor. Hopes for a therapy for such patients are not high, as little is known about the factors that control tumor progression and metastasis.

However, Javed Khan and colleagues, at the National Cancer Institute, Bethesda, have now determined that the protein FGFR4 has a role in RMS progression and have data suggesting that it might be a good drug target for the treatment of individuals with RMS.

In the study, higher levels of expression of the FGFR4 gene were found to be associated with advanced-stage cancer and poor survival.

Conversely, reducing FGFR4 expression in a human RMS cell line decreased its ability to grow and metastasize when transplanted into mice. Further analysis identified mutations in the FGFR4 gene in 7.5% of human RMS tumor samples analyzed. When two of the FGFR4 mutants generated by these genetic mutations were analyzed further, they were found to be constitutively activated forms of FGFR4 that increased the proliferative, invasive, and metastatic capacities of a murine RMS cell line.

Importantly, treatment with a pharmacologic inhibitor of FGFRs made the murine RMS cells expressing the FGFR4 mutants very susceptible to

death, leading the authors to suggest that targeting FGFR4 might be of therapeutic benefit in RMS.

More information: View this article at: www.jci.org/articles/view/3970 … 140858eba01ab916a067

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