The genesis of this work was that we observed the expression of a protein (named Myogenin) in alveolar rhabdomayosarcoma (RMS). RMS is an aggressive pediatric soft tissue cancer that retains some features of skeletal muscle. Common tumor sites are structures of the head and neck, the urogenital tract, and the limbs. Myogenin protein is normally associated with “terminal differentiation” of muscle cells which is a state in which normal muscle cells stop dividing. However, in RMS the cells do not stop dividing and are therefore cancerous. We found that, despite being present in the cells, the Myogenin protein is inactivated by a modification mediated by another protein called Glycogen Synthase Kinase 3 beta (GSK3b). Importantly, we observed that pharmacological inhibition of GSK3b reduced the tumor causing properties of RMS cells. Interestingly, electrical stimulation of cells which makes the muscle cells contract also reduces GSK3b activity. These observations suggest that pharmacological or possibly contraction mediated GSK3b inhibition might prove a potential therapy for patients with alveolar rhabdomyosarcoma.

Reference: Dionyssiou MG, Ehyai S, Avrutin E, Connor MK, McDermott JC. Glycogen synthase kinase 3β represses MYOGENIN function in alveolar rhabdomyosarcoma. Cell Death Dis. 2014 Feb 27;5:e1094.

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