THE HARTWELL FOUNDATION

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Directing Stem Cells to the Fat Cell Lineage to Treat Infantile Hemangiomas

Infantile hemangiomas are vascular tumors found in ~5-10% of infants. Hemangiomas, commonly referred to as "strawberry marks," are the most common tumors of infancy. These blood-vessel tumors are found on the skin layer at various locations throughout the body and present with a deep reddish color. They exhibit a predictable clinical course that is characterized by early growth and proliferation of endothelial (blood vessel-forming) cells and pericytes (stem cells that line the blood vessels), followed by spontaneous shrinkage into fatty tissue cells called adipocytes. Infantile hemangiomas are generally considered benign. However, upwards of 25% of infantile hemangiomas may produce significant complications, including interference with vital structures (e.g. eyes, mouth, or genitals), bleeding, and ulceration. Some hemangiomas produce excess amounts of a protein that degrades thyroid hormone, causing many affected infants to develop hypothyroidism, an extremely serious complication that produces neurological damage. Hemangiomas that are large in size, particularly those on the face, create undue psychological stress, especially in the context of social interactions. Current treatment options for hemangiomas include surgery, laser therapy, and prescription drug treatments, including propranolol and oral systemic corticosteroids. While effective, propranolol has side undesirable effects that can include symptomatic hypoglycemia, hypotension, bronchial hyperactivity, seizure, restless sleep, and constipation. Corticosteroid treatment is relatively less effective and also comes with undesirable side effects such as immune suppression, hypertension, bone demineralization, sleep disturbance, weight gain, irritability, personality change, and gastrointestinal irritation. Unfortunately, the development of safe and effective treatments for hemangiomas has been hampered by a lack of understanding their origin and the mechanism that drives their natural involution into fat cells. In contrast to the current paradigm to eradicate tumor cells by inducing cell death, Rana proposes an innovative but risky therapeutic strategy based upon his discovery of a mechanism that controls terminal differentiation of hemangioma cells into fat cells. He hypothesizes that the committed preadipocyte within the involuting hemangioma is also a specialized adipocyte precursor. Using next-generation RNA sequencing, together with cellular and animal models of hemangiomas and their resident pre-adipocytes, he proposes to target the tumor-residing pre-adipocyte to accelerate the natural adipocyte involution process. If Rana is successful, his approach will advance clinical translation with the potential for children to overcome the debilitating effects of a hemangioma, a technical advance that may also strategically impact interventions in diabetes, heart disease, cancer, and obesity.