THE HARTWELL FOUNDATION

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Engineering a Construct to Recover Endocrine Function in Children with Ovarian Failure

Female survivors of childhood cancer represent a rapidly growing population of patients who experience premature ovarian failure (POF). This patient population is growing due to highly effective interventions, resulting in over 80% long-term survival. However, chemotherapy, radiation and surgery can all contribute to ovarian failure, reducing the principal female hormones, estrogen and progesterone. Estrogen is required for normal female development and plays a very important role in maintaining the health of all the connective tissues in the body, including blood vessels, skin, ligaments and bones. Progesterone controls a woman's menstrual cycle. Beginning at puberty, estrogen maintains bone strength and protects against heart disease, while defining female gender identity. The loss of estrogen is also associated with deterioration of the blood vessels in the brain, which may lead to strokes. Young girls affected by ovarian failure are more prone to gum disease, tooth loss and cataracts. Up to 40% of young girls who experience POF will endure premature menopause syndrome. The effects of estrogen deficiency on a growing girl are devastating because they substantially limit her ability to “graduate” into young adulthood. The negative effects of POF that create short physical stature and altered body image ultimately interfere with physical well-being, as well as psychosocial and sexual development, including fertility. The only available therapy is artificial hormone replacement therapy, which although extensively studied in menopausal adult women the long-term safety data in children is scant. For example, the danger with prolonged exposure to hormonal replacement therapy in adults has been linked to increased risk of breast cancer and venous thrombosis (blood clots). The risk of synthetic hormones is attributed to unnaturally elevated levels following their administration, as opposed to the normal physiologic levels maintained by the finely tuned feedback mechanism provided by healthy ovaries. No alternative form of therapy for POF is available to young girls. To meet this unmet need, Ariella proposes to develop a follicle transplant strategy that will provide delivery of natural estrogen at physiologic levels, while simultaneously reestablishing hormonal feedback regulation. Her innovation is to develop a bioengineered matrix that will support follicle survival and function, which in an immune-privileged environment will prevent rejection by the recipient while continuing to produce estrogen and progesterone under conditions similar to normal physiologic regulation. If she is successful, young girls who are forced to endure ovarian failure as the result cancer treatment strategies will be able to not only avoid the deleterious effects of estrogen and progesterone deficiency, but the risks associated with synthetic hormonal replacement therapy; thus experiencing normal development and puberty, and an otherwise healthy life.