Title: How the cells that make insulin adapt to puberty

Researchers:

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Research area: Type 2 diabetes

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Summary:

The rise in obesity in children is a major health issue, and as a result, the age at which type 2 diabetes occurs has been steadily decreasing in recent years. Children who are overweight during puberty have an increased risk of developing type 2 diabetes later in life. The reasons why pubertal obesity confers a type 2 diabetes risk are unknown.

There are many hormonal changes that occur during puberty. One such change is a decrease in the ability of insulin to promote the storage of energy into its target tissues. This transient so-called “insulin resistance” is normally compensated for by an increase in the production of insulin from the pancreas, due in part to the replication of the beta cells that secrete insulin. Surprisingly, very little is known about the mechanisms by which beta cells adapt to puberty. The objectives of this project are to discover the cellular mechanisms underlying beta-cell adaptation to puberty, and to ascertain whether these mechanisms are altered in an obese environment.

Based on preliminary findings obtained by our group, we hypothesize that beta-cell mass expansion during puberty involves two signaling pathways, the growth hormone/serotonin pathway and the sex hormone pathway. To test this hypothesis, we will first examine in male and female rat models and human samples the contribution of the growth hormone/serotonin pathway by manipulating the expression of the receptor for growth hormone and the enzyme that makes serotonin. Second, using similar strategies we will test the implication of the sex hormones (testosterone and estrogens). Finally, we will feed rats with a diet enriched in fat and examine whether the pathways studied above are impaired.

This project will provide detailed information as to how the pancreatic beta cell adapts to insulin resistance during puberty, and how these mechanisms are affected by obesity. These findings will help devise strategies to curb the alarming increase in type 2 diabetes in young adults.