

Title: Assessing the Potential of TSI for Treating Hyperparathyroidism

Abstract:

The purpose of the proposal is to explore the suitability of the Targeted Secretion Inhibitor (TSI) platform as a novel treatment of hyperparathyroidism.

Primary hyperparathyroidism is a common endocrine disorder caused by overproduction of parathyroid hormone (PTH) from the parathyroid glands. Recent trends in the US suggest that the incidence of the disease is >100,000 new cases annually, predominantly affecting post-menopausal women. In the majority of patients, the culprit lesion is an adenoma that developed in one of the four parathyroid glands and overproduces PTH. This leads to high blood calcium and high urine calcium, which can result in kidney stones, kidney failure, and osteoporosis. The only curative approach is surgical removal of the adenoma, but some patients either do not wish to undergo neck surgery or are poor surgical candidates. Medical therapy using the oral calcium-sensing agonist cinacalcet fails to improve skeletal health and is rarely used in practice because of significant gastrointestinal side effects including nausea. Therefore, new therapies are needed. Here, we are exploring the potential of the TSI platform to inhibit PTH secretion, and we propose a multi-step project. The pilot grant would permit completion of the first steps: determining which SNARE proteins are expressed in human parathyroid adenomas using RNA-seq and Western blot; searching for proteins expressed in human parathyroid adenoma that are suitable as TSI targets; developing a primary cell culture system using fresh human parathyroid adenoma.