

## **PRESS RELEASE**

### **Researchers Discover New Genes Regulating Hormone Action in Humans**

A team of investigators including Mount Sinai's Dr. Paul Walfish has discovered several new genes in the human genome which are essential for the action of thyroid hormone in humans. These observations provide another step towards understanding the molecular mechanisms regulating not only thyroid hormone action but also for other hormones such as estrogen, testosterone and retinoic acid (Vitamin A). The study – an international collaboration that included scientists from Dr. Walfish's lab at Mount Sinai Hospital, Toronto as well as Laval University, Quebec PQ, The University of New Hampshire, Durham, North Carolina USA and the Methodist Hospital Research Institute, Houston, Texas USA – was published in the November 23<sup>rd</sup> issue of the Proceedings of the National Academy of Sciences. It is the first study performed using a modification of a yeast synthetic genetic array analysis (SGA) method to discover potential homologous human genes which are essential for thyroid hormone action. Using this SGA model system, 384 yeast genes were isolated that regulate gene transcription and chromatin remodeling in the context of a reporter gene system which has reconstituted hormone action. This novel functional genomic technique provided an unbiased method to discover human proteins essential for gene activation by thyroid and several other hormones. As a proof of principle, one of these genes, yeast CCR4, initially discovered by Dr. Clyde Denis at the University of New Hampshire (one of the senior authors) was further assessed in a human cell based system (HeLa cells) and was shown to have an identical functional role in facilitating gene activation by thyroid hormone as well as several other hormones in the family of hormone-dependent nuclear receptor proteins. These findings have also confirmed that specific genes have

been evolutionarily conserved between yeast and humans and that mutations in such candidate genes in humans could thereby be a potential site for impaired hormone action.

Dr. Paul Walfish, who was the Principal Senior Investigator, in this study is a Professor Emeritus of the Institute of Medical Sciences, School of Post Graduate Studies, University of Toronto and a Senior Consultant, Endocrine Division and the Joseph & Mildred Sonshine Family Centre for Head and Neck Diseases at Mount Sinai Hospital, Toronto.