

P051 Studies on the Transcriptional Regulation of Cholesterol 24-Hydroxylase: A key regulator of brain cholesterol homeostasis
Yoshihiko Ohyama^{S*}, Steve Meaney^{*}, Maura Heverin^{*}, Anat Brafmant[†], Millicent Shafir[†], Ulla Andersson^{*}, Maria Olin^{*}, Gösta Eggertsen^{*}, Ulf Diczfalusy^{*}, Elena Feinstein[†] and Ingemar Björkhem

**Division of Clinical Chemistry, Department of Laboratory Medicine, Karolinska Institutet at KUS - Huddinge;
SDepartment of Mathematical and Life Sciences, Graduate School of Science, Hiroshima University, Japan; †Quark Biotech, Inc, Fremont, CA 94555, USA*

Recent studies have suggested that alterations in brain cholesterol homeostasis are important for the development and/or progression of Alzheimer's Disease. Brain cholesterol balance is maintained by a combination of recycling, production and excretion. Conversion of cholesterol into 24S-hydroxycholesterol by the cholesterol 24-hydroxylase (CYP46A1) is the most important mechanism for cholesterol excretion from the brain.

Here we describe the characterization of the transcriptional regulation of cholesterol 24-hydroxylase. The promoter was extensively tested using a variety of deletion constructs and a range of known small molecule regulators of lipid homeostasis. Transcriptional regulation of CYP46A1 *in vivo* was explored using a sterol deficient mouse model (dhcr24 null mouse) in which almost all the substrate had been replaced with desmosterol. Compared to heterozygous littermates there was no statistically significant difference in the mRNA levels of Cyp46a1. The apparent lack of significant transcriptional regulation is discussed in relation to the turnover of brain and neuronal cholesterol, and its potential impact for neurodegenerative conditions.