

32

EHT

Judging Dept.

Guoyu Ling

Student

EHT

5

Xinxin Ding

Dept or Program Years in program

Mentor

Identification and characterization of transcription factors interacting with the NPTA element of the cytochrome P450 2A3 (CYP2A3) gene

Author (s)

Guoyu Ling, Richard M. Gronostajski & Charles Hauer

CYP2A3, and its mouse and human orthologs (CYP2A5 and CYP2A13, respectively), are expressed preferentially in the olfactory mucosa. We previously found that a nuclear factor 1 (NFI)-related regulatory element (named NPTA element) in the proximal promoter region of the CYP2A3 gene is critical for transcriptional activation in vitro, and therefore suggested that this element may be important for the tissue-selective gene expression. In this study, DNA-affinity purification was applied to isolate the NPTA-binding proteins from rat olfactory mucosa. Mass spectral analysis demonstrated that isoforms corresponding to all four NFI genes are present in the purified NPTA-binding fraction, with NFI-A being the most abundant. However, it was difficult to definitively identify the specific isoforms present because most peptides detected can be attributed to multiple isoforms. Subsequent studies led to the identification of a novel NFI-A isoform which has a truncated transactivation/repression domain. A luciferase reporter construct driven by the CYP2A3 promoter is being used to determine the roles of this short NFI-A isoform as well as that of NFI-A2 in CYP2A3 expression in a number of cell lines; the NFI-A2 isoform, which is restricted to the olfactory mucosa, was recently found to activate the NPTA element in yeast one-hybrid assays.