

Press Release

Cytochroma Inc. Discovers New Retinoic Acid Metabolizing Cytochrome P450

New Discovery Completes The CYP26 Gene Family

MARKHAM, Ontario, Canada – August 21, 2003 - Cytochroma Inc., announced today that it has discovered a new gene named CYP26C which encodes a retinoic acid metabolizing enzyme.

"Our discovery of the third member of this family of cytochrome P450s gives us an exclusive advantage to develop CYP26 specific and pan inhibitors for a wide range of potential applications", stated Dr. Robert Foldes, President & CEO.

Cytochroma demonstrated that CYP26C, and not CYP26A or CYP26B, metabolizes *9-cis* retinoic acid. All three members of the CYP26 family metabolize *all-trans* retinoic acid. It is well known that *9-cis* and *all-trans* retinoic acid function as potent inducers of cell differentiation and inhibitors of cell proliferation. By developing compounds which act on the CYP26 gene family, treatment of diseases such as cancer, as well as skin diseases such as acne and psoriasis, may be possible.

To look at possible diseases specifically linked to CYP26C expression, Dr. Martin Petkovich, Chief Scientific Officer for Cytochroma, has recently published work on the expression pattern in mouse embryos for CYP26C. Knowing where CYP26C is normally expressed is the first step in determining which diseases may be associated with this gene. Dr. Petkovich's work has shown expression for CYP26C in the hindbrain, inner ear and tooth buds during embryonic development.

"Evidence that CYP26 enzymes are involved in brain function is very compelling", commented Dr. Martin Petkovich. "The role of retinoic acid in controlling neuronal differentiation is well established and CYP26 inhibitors may be useful in promoting differentiation of neuronal stem cells as a possible approach to treat various disorders of the central nervous system."

CYP26 inhibitors are expected to raise endogenous levels of both *all-trans* and *9-cis* retinoic acid in cells expressing the enzyme and thereby activate both RAR and RXR nuclear receptor pathways in a cell- and tissue-specific fashion.

Cytochroma is currently pursuing discussions with potential strategic partners to further develop this exciting discovery.

Cytochroma Inc. is a leader in the discovery and development of novel small molecule drugs regulating cytochrome P450s to treat skin diseases and cancer with enhanced efficacy and improved safety margins. To date, Cytochroma's drug discovery program has identified modulators of retinoic acid and calcitriol metabolism as drug candidates for the treatment of skin diseases and cancer. For more information, please visit www.cytochroma.com.

