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Citation: Finn, Robert (2011) Cytochrome P450 Monooxygenase Complex and Skin Development. In: Northumbria Research Conference, 5-6 May 2011, Northumbria University, Newcastle-upon-Tyne.

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Abstract for Oral Presentation/Paper

Cytochrome P450 Monooxygenase Complex and Skin Development.

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Cytochromes-P450 (CYPs), the first line-defence in the detoxification of drugs/harmful chemicals, play a role in various biological processes such as fatty acid metabolism. For these functions, CYPs form a complex with P450-oxidoreductase (POR) and cytochrome-*b*₅ (*cytb*₅). To investigate this complex in more detail, we developed mouse models where either POR or *cytb*₅ was knocked out in the liver or the organism as a whole. Results show the absence of POR/*cytb*₅ has a dramatic effect on all CYP functions^{1, 2}. In studies involving knockout *cytb*₅ mice, a role in skin development was identified³. Changes observed were very similar to patients suffering from ichthyosis skin disorders⁴. These disorders are associated with loss of very long chain fatty acids. The CYP4 family function in the production of these fatty acids, therefore the defects observed in these mice maybe due to disrupted CYP4 activity. Supporting this hypothesis, genetics disruptions in CYP4F22, have been identified in patients suffering from lamellar ichthyosis⁵. A role for this new CYP in very long chain fatty acid production in the skin remains unproven as does a link between its function and *cytb*₅. This paper will report these findings and the directions which will be taken to decipher these links.

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3. Finn, R.D., *et.al.* (2010) Cytochrome *b*₅ null mouse: a new model for studying inherited skin disorders and the role of unsaturated fatty acids in normal homeostasis. *Transgenic Research*. DOI: 10.1007/s11248-010-9426-1
4. Akiyama M & Shimizu H (2008) An update on molecular aspects of the non-syndromic ichthyoses. *Exp Dermatol* 17(5): 373-382.
5. Lefevre, C., *et al.* (2006) Mutations in a new cytochrome P450 gene in lamellar ichthyosis type 3. *Hum Mol Genet* 15(5): 767-776.