

## Function Of Psoriasis Susceptibility Gene CCHCR1

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**Inkeri Tiala, MSc, defended her PhD thesis on May 20<sup>th</sup>, 2009 in Helsinki. The opponent was Associate Professor Kaisa Tasanen-Määttä from the Department of Dermatology, University of Oulu, Finland. The thesis was supervised by Professor Juha Kere from the Department of Medical Genetics, University of Helsinki, Folkhälsan Institute of Genetics, and Department of Biosciences and Nutrition at Novum, Karolinska Institutet, Huddinge, Sweden, and Associate Professor Outi Elomaa from the Department of Medical Genetics, University of Helsinki. The thesis book can be found in the internet at: <http://urn.fi/URN:ISBN:978-952-10-5482-2>.**

Psoriasis is a chronic skin disease characterized by abnormal keratinocyte proliferation and differentiation, neoangiogenesis and inflammation. Its etiology is multifactorial, as both the environmental and genetic factors have an important role in the pathogenesis of psoriasis. Anyhow, the exact disease mechanism behind psoriasis still remains unknown. The most important genetic susceptibility region for psoriasis has been located to PSORS1 locus in chromosome 6. The area includes multiple good candidate genes but the strong linkage disequilibrium between them has made genetic studies difficult. One of the candidate genes in PSORS1 is CCHCR1, which has a psoriasis-associated gene form CCHCR1\*WWCC. The aim of this study was to elucidate the function of CCHCR1 and its potential role in the pathogenesis of psoriasis.

In this study, transgenic mice expressing either the healthy or psoriasis-associated gene form of CCHCR1 were engineered and characterized. Mice were phenotypically normal but their gene expression profiles revealed many similarities to that observed in human psoriatic skin. In addition, the psoriasis-

associated gene form had specific impacts on the expression of many genes relevant to the pathogenesis of psoriasis. We also challenged the skin of CCHCR1 transgenic mice with wounding or 12-O-tetradecanoylphorbol-13-acetate (TPA). The experiments revealed that CCHCR1 impacts on keratinocyte proliferation by limiting it. In addition, we demonstrated that CCHCR1 has a role in steroidogenesis and showed that both CCHCR1 forms promote synthesis of steroids. Also many agents relevant either for steroidogenesis or cell proliferation were shown to regulate the expression level of CCHCR1.

The present study showed that CCHCR1 has functional properties relevant in the context of psoriasis. Firstly, CCHCR1 affects proliferation of keratinocytes as it may function as a negative regulator of keratinocyte proliferation. Secondly, CCHCR1 also has a role in steroidogenesis, a function relevant both in the pathogenesis of psoriasis and regulation of cell proliferation. This study suggests that aberrant function of CCHCR1 may lead to abnormal keratinocyte proliferation which is a key feature of psoriatic epidermis.