



“CHARGEd with neural crest defects”

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AUTHORS AND THEIR CONNECTION TO THE CHARGE SYNDROME FOUNDATION:



Silke Pauli, MD, is a Human Geneticist at the Institute of Human Genetics, University Medical Center, Göttingen, Germany.

Her main areas of interest are clinical and molecular aspects of CHARGE syndrome and related disorders. Among others, she has collaborated with Conny van Ravenswaaij-Arts' team in the Netherlands.



Ruchi Bajpai, PhD, is an Assistant Professor at the Center for Craniofacial and Molecular Biology of the University of Southern California, Los Angeles. **Ruchi was a recipient of a 2014 CHARGE Syndrome Foundation Pilot Grant**, which she used in part to develop human stem cell and Xenopus (frog) models to understand neural crest development in CHARGE syndrome.

Currently she uses both human cells and animal models to gain insight into CHARGE syndrome in hope of developing potentially therapeutic strategies. She has presented her research at Professional Day of the 2015 CSF conference.



Annette Borchers, PhD, is a professor of Zoology at the University of Marburg, Germany with a longstanding interest in the development of the neural crest and in particular the molecular mechanisms controlling neural crest migration.

In recent years she also focused on the epigenetic control of these processes, including in CHARGE syndrome animal models.

SUMMARY OF THE PAPER:

Abstract: Neural crest (NC) cells in the embryo give rise to many different tissues, including cartilage, bone, smooth muscle, pigment, and endocrine cells as well as neurons and glia. Abnormalities in neural crest-derived tissues result in many of the features of CHARGE syndrome (CS). Mutations in the *CHD7* gene can cause CS in humans. Animal models of

CS clearly show a role for *Chd7* in NC development. In this paper, the authors summarize the current understanding of the function of *CHD7* in neural crest development and discuss possible links of CS to other developmental disorders.

Additional summary: *CHD7* is one of a category of Chromodomain Helicase DNA-binding proteins which have the ability to use the energy released from ATP hydrolysis to do *mechanical work* in the cell, like physically moving nucleosomes or changing DNA from tightly packed to loosely packed, which has the effect of regulating the expression of a multitude of additional genes. Because so many features of CS involve the NC, they and other researchers have looked closely at how NC cell processes are affected by changes in *Chd7* – both in animal models and cell systems in the lab. The paper includes descriptions of studies involving mouse, chick, zebrafish, clawed frog and fruit fly. One figure shows corresponding features (e.g. eyes, brain, heart) in children with CS and frog tadpoles. Another figure illustrates the *CHD7* multiprotein complexes which may represent the molecular link between CHARGE and other syndromes with clinical overlapping phenotypes such as 22q deletion syndrome and Kabuki syndrome.

Examining how *CHD7* works at a cellular level helps guide thinking about potential therapies. Mouse models have been developed which have mutations in other genes which appear to reverse some of the effects of *Chd7* mutations. Studies such as these may eventually lead to therapies or treatments for some features of CS. That said, the functions of *CHD7* are many and complex and only beginning to be understood.

WHAT DOES THIS MEAN TO FAMILY/PERSON WITH CHARGE?

This is basic research at its finest. It will not make any difference to individuals with CS in the near future, but holds the most promise for eventually understanding not only CS and *CHD7* but epigenetics and embryology in general. We are fortunate that *CHD7* is such a fascinating gene, with many extremely skilled researchers interested in teasing out its secrets.

SHOULD I READ IT? SHOULD ONE OF MY DOCTORS READ IT?

If you want an idea of the really exciting basic research being funded by your contributions to the CHARGE Syndrome Foundation, definitely take a look at this paper. This is not one that will contribute to the everyday management of CS, but if you are fascinated by *CHD7* and how one gene can be responsible for do so many things, you might want to take a look. Don't be put off by the lab jargon and alphabet soup - read the introduction and conclusion look at the figures. If that intrigues you, find the bits that very nicely explain how this sort of research is done and how conclusions are drawn.

FULL CITATION:

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