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Science

My research interest is in the identification of genes involved in neurodegenerative disease processes. For this purpose I integrate functional genomic and molecular genetic approaches in frontotemporal lobar degeneration (FTLD), a group of neurodegenerative diseases of the frontal and temporal brain lobes. My recent research excluded the tau gene (*MAPT*) and identified granulin (*GRN*) as a major player in the pathogenesis of the neuropathological FTLD subtype characterized by TDP-43 inclusions (FTLD-TDP). This, for the first time, offered a lead for cell biological studies of FTLD-TDP. Now, I focus on the identification of modifier genes contributing to the age-related disease penetrance associated with *GRN* mutations. Therefore, transcriptome analysis of patients of an extended *GRN* family is correlated with molecular genetics and proteomics in the same family. Further, using interactome analyses, I aim to identify molecular pathways affected in FTLD and to investigate the genetic role of other genes of these pathways in neurodegeneration. Together, these studies aim to provide new tools to elucidate the cell biology of FTLD and identify molecular targets for developing therapeutics. Knowledge obtained in FTLD may apply to related neurodegenerative diseases, such as Alzheimer disease (AD), Parkinson's disease and motor neuron diseases. The identification of novel disease genes also contributes to improved molecular diagnostic protocols and more accurate differential diagnoses. Finally, I am curator of the AD&FTD Mutation Database (http://www.molgen.ua.ac.be/ADmutations), the online reference database for mutations in AD- and FTLD-related genes.

Selected Publications

Cruts,M., Van Broeckhoven,C.: Loss of progranulin function in frontotemporal lobar degeneration. Trends in Genetics 24: 186-194 (2008) (I.F.: 9.950)

Cruts,M., Gijselinck,I., van der Zee,J., Engelborghs,S., Wils,H., Pirici,D., Rademakers,R., Vandenberghe,R., Dermaut,B., Martin,J-J., van Duijn,C., Peeters,K., Sciot,R., Santens,P., De Pooter,T., Mattheijssens,M., Van den Broeck,M., Cuijt,I., Vennekens,K., De Deyn,P., Kumar-Singh,S., Van Broeckhoven,C.: Null mutations in progranulin cause ubiquitine-positive frontotemporal dementia linked to chromosome 17q21. Nature 442: 920-924 (2006) (I.F.: 29.273)

Cruts,M., Rademakers,R., Gijselinck,I., van der Zee,J., Dermaut,B., De Pooter,T., De Rijk,P., Del-Favero,J., Van Broeckhoven,C. Genomic architecture of human 17q21 linked to frontotemporal dementia uncovers a highly homologous family of low copy repeats in the tau region. Human Molecular Genetics 14: 1753-1762 (2005) (I.F.: 7.764)

Cruts,M., van Duijn,C.M., Backhovens,H., Van den Broeck,M., Wehnert,A., Serneels,S., Sherrington,R., Hutton,M., Hardy,J., St. George-Hyslop,P.H., Hofman,A., Van Broeckhoven,C. Estimation of the genetic contribution of presenilin-1 and -2 mutations in a population-based study of presenile Alzheimer disease. Human Molecular Genetics 7: 43-51 (1998) (I.F.: 9.307)

Cruts,M., Backhovens,H., Wang,S.-Y., Van Gassen,G., Theuns,J., De Jonghe,C., Wehnert,A., De Voecht,J., De Winter,G., Cras,P., Bruyland,M., Datson,N., Weissenbach,J., den Dunnen,J.T., Martin,J-J., Hendriks,L., Van Broeckhoven,C.: Molecular genetic analysis of familial early-onset Alzheimer's disease linked to chromosome 14q24.3. Human Molecular Genetics 4: 2363-2371 (1995) (I.F.: 5.273)

All publications