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Molecular diagnosis of multifactorial psychiatric diseases: functional validation of identified gene variants using nanobodies coupled to fluorescent diamond nanoparticles

Project coordinator
Michel Simonneau
michel.simonneau@inserm.fr
Institut National de la Santé et de a Recherche | Médicale-INSERM) | Center for Psychiatry & Neurosciences | Paris | France

Acronym

NanoDiaMed

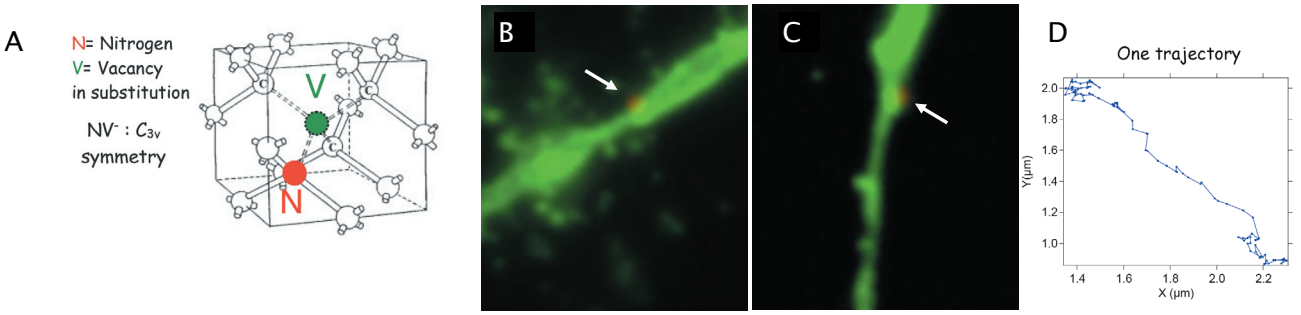
Project partners

- Aiden CORVIN | Institute of Molecular Medicine - Trinity College | Dublin | Ireland
- Anke KRÜGER | Julius-Maximilians-Universitaet Wuerzburg | Germany
- François TREUSSART | Laboratoire de photonique quantique et moléculaire ENS Cachan | France
- Carlo SALA | Institute of Neuroscience | CNR | Milano | Italy
- GATC Biotech AG | Konstanz | Germany

Abstract

We aim to validate psychiatric diseases-associated gene abnormalities using novel nanoprobes (FNDs).

Schizophrenia is a chronic, severe, and disabling brain disorder that has affected people throughout history. The illness occurs in 1 percent of the general population, but it occurs in 10 percent of people who have a first-degree relative with the disorder, such as a parent, brother, or sister, indicating a strong genetic component. Recent large-scale studies were able to characterize the genetic architecture of these psychiatric diseases that include common variants and rare variants. By combining expertise in human genetics, deep sequencing, chemistry of nanoprobes, nanobodies, neurobiology and novel microscopies, this study will have to identify novel rare variants and to validate their functional impact using novel nanoprobes based on fluorescent nanodiamonds coupled to antibodies in order to quantify parameters linked to neuronal function such as dendrite and dendritic spine trafficking, movements of receptors at synapses



Strategies to validate psychiatric diseases-associated gene abnormalities using novel nanoprobes
A: schematic representation of a fluorescent nanodiamond (fND).
B and C: visualization of fNDs (white arrows; visualized in red) in dendritic spines (visualized in green by a beta-actin-GFP transgene) that start to be formed in cultured cortical mouse neurons imaged with TIRF microscopy.
D. quantification of dendritic trafficking using fNDs inside dendrites of live cultured cortical mouse neurons imaged with TIRF microscopy.