# High Content Screening of synucleinopathy in primary cortical neurons

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**Résumé**

The initiation and spread of synucleinopathy are considered the key steps in the development of several neurodegerative disease such as PD, MSA, DLB and. These molecular events could be induced in primary cultures of cortical neurons by treating these latter with preformed fibrillar assemblies of recombinant a-synuclein (PFFs). However, several barriers have slowed down the adoption of this type of assay for screening purposes: (i) the ease and reliability of the isolation and culture protocols capable to insure long term survival ($>$ 21 DIV) of primary cortical neurons in a 96 well culture format, (ii) the batch-to-batch variability of artificial recombinant PFFs in terms of bioactivity, (iii) the relative lack of characterization of the anti-synuclein antibodies for a specific use in non-denaturing conditions such as immunofluorescence imaging. We worked at raising specifically these barriers, in particularly making a comprehensive comparative work on synuclein antibodies for their use in high content screening. This systematic analysis represents a very important step to identify a relevant read out for quantifying the progression of synucleinopathy in vitro, leading to the setting up of a high content screening assay that can be routinely used to characterize the bioactivity of test-compounds. Not to mention that it could also reveal new clues on alpha synuclein biology and pathology, as we show here by comparing the effects of the expression of a set of pathological or experimentally generated mutations of alpha synuclein.

**Mots-Clés:** high content screening, synucleinopathy, synuclein, neuron

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