**Proposal for Radboud AI for Health course project**

*Project proposals must be in English. Images may be added.*

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| Title: iPSC lines from patients with neurodevelopmental disorders |
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| Applicant |
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| Description of the clinical problem that must be solved *(max 400 words)* |
| Patient-derived iPSC models are gaining momentum as preclinical models for studying disease mechanisms, drug screening and validation. They may eventually largely replace animal studies. The group of Nadif Kasri has previously established the NGN2 transduction protocol for fast and robust differentiation of human iPSCs into functional excitatory neurons in 2D culture dishes, showing electrophysiological phenotypes that are relevant to neurodevelopmental disorders (Mossink et al. Stem Cell Reports, 2021). However, subsequent transcriptomics profiling also showed considerable variability between different iPSC lines from patients with the same mutation (Klein Gunnewiek et al, Stem Cell Reports 2021; Verboven et al. in preparation). The considerable variability observed between experiments, clones and between patients is partly attributable to a lack of technological standardization but may also reflect biological heterogeneity between cells and individuals. Here, we would like to showcase how multi-omics characterization of iPSC lines leads to a better understanding of sources of variability, and aids in distinguishing disease-relevant from other sources of variation. It will generate an important benchmark for future studies involving neuronally differentiated iPSCs and improve the design of those studies in a wide range of neurodevelopmental disorders. The efforts are also likely resulting in the collection of multi-omics evidence for druggable pathways and the identification of disease biomarkers. |

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| Description of the AI challenge, task and/or research question(s) *(max 300 words)* |
| Due to the large dataset with multi-omics nature. It is necessary for mapping disease pathways across different disorders using pathway enrichment strategies and multilayer network analyses, including multilayered diffusion propagation methods (random walk, heat diffusion) that make combined use of established knowledge networks (for example containing the interactions between genes, proteins and metabolites) and the multi-omics data obtained . |

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| Description of the data set that will be used.   * Please provide detailed information about the type of data, the number of patients/scans/measurements etc. * Is the data annotated / are ground truth labels available? * Do you have access to the data? * Do you have permission to use the data? * Could colleagues at RadboudUMC use the data in the Digital Research Environment? * Could participants from outside RadboudUMC use the data? *(max 450 words)* |
| The data is consisted of analysis from different omics levels. Genomics, proteomics, metabolomics and lipidomic. There are 3 patients and one control per cell lines, each cells lines underly one diseases. All analyses are done in triplicates.  The data will be generated by internal and external partners. The data will be annotated and delivered by end of October. I will have access to the data and persmission to use the data. Radboud employee can use the data within the DRE or outside. External participants accessibility is to be decided. |

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| What will be the main result or innovation of the project? How could this innovation contribute to making an impact on healthcare in Radboudumc in the longer term? *(max 300 words)* |
| The result and impact are explained in the description. The neurological disorders are rare, and thus provide protential insights on how to find the eventual personalized treatment. |