**EPFL Life Sciences seminar series in Lausanne**

*Meeting the therapeutic challenge of Huntington's disease*

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Huntington's disease (HD) is a devastating autosomal dominantly inherited neurodegenerative disease for which there is currently no effective disease modifying therapy. The genetic predictability of HD provides an opportunity for early therapeutic intervention many years before overt symptom onset and at a time when reversal or prevention of neural dysfunction may still be possible. As HD is monogenetic, fully penetrant, and characterised by a long premanifest phase, it is emerging as a potential model for studying therapeutic intervention in other neurodegenerative conditions such as Alzheimer's or Parkinson's disease where no preclinical diagnostic tests exist. In addition, HD manifests with a broad range of clinical symptoms and signs, many of them common to these other diseases, and involves widespread pathology throughout most of the brain. Understanding of HD pathogenesis is evolving, and I will present our recent findings on identifying novel genetic modifiers of disease progression, and their relevance for designing new therapeutics. In the main body of my lecture, I will give an overview of important approaches in development for targeting mutant HTT DNA and RNA, and in particular I will focus on the recent successful phase 1b/2a clinical trial testing the effects of RG6042 (formerly known as IONIS HTT Rx) in patients with early Huntington's Disease and present the results of the first successful HTT-lowering drug trial.