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A *Drosophila* high-throughput drug screening platform identifies inhibitors of misregulated alternative splicing events in myotonic dystrophy

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An automated *in vivo* screening platform for the identification of molecules able to modulate alternative splicing events linked to human disease is introduced. The screening assay is based on the generation of transgenic flies that express a spliceosensor construct, this is, a minigene whose alternative splicing is coupled to the production of the luciferase reporter. For the *Drosophila*-based assay we took advantage of the fact that flies were able to closely mirror missplicing events associated to myotonic dystrophy type 1 (DM1), which is the first described human spliceopathy. The design of the high-throughput screening pilot study also implemented recent advances in fly assay miniaturization and automation, allowing a top screening speed of 1,000 compounds per week. Together, more than 15,000 small molecules, which constitutes one of the largest *in vivo* pharmacological screening to date were screened and identified more than 30 primary hits, several showing promising anti-DM1 properties according to their putative mechanisms of action and effect on molecular hallmarks of the disease. The *Drosophila*-based tools here described are valuable and flexible resources for innovative drug discovery on human pathologies originating from alternative splicing misregulation.

Biography

Ruben Artero is Associate Professor of Genetics at the University of Valencia-INCLIVA Biomedical Research Institute, where he leads the Translational Genomics group dedicated to discovering mechanisms of pathogenesis of human genetic diseases as well as to design novel *Drosophila* models for *in vivo* drug discovery, particularly in myotonic dystrophy, spinal muscular atrophy and breast cancer. Before his interest in biotechnology he performed basic research in the field of developmental genetics studying *Drosophila* myogenesis both in University of Valencia and in the Memorial Sloan-Kettering Cancer Center (NY, USA), where he spent some six years as postdoctoral fellow. He is co-founder of the Genera Biotech company, scientific advisor of ValentiaBioPharma and inventor in four patents. He has participated in 30 international journal research publications and serves as academic editor for the PLoS ONE journal.

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