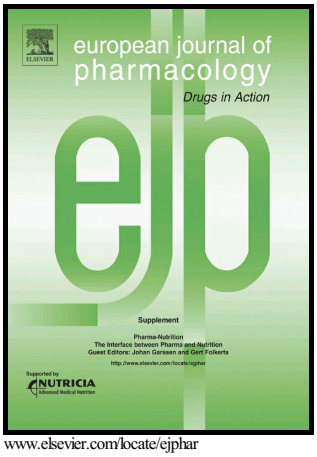

www.elsevier.com/locate/ejphar

Towards the virtual human patient. Quantitative Systems Pharmacology in Alzheimer's Disease

Hugo Geerts, Athan Spiros, Patrick Roberts, Robert Carr

PII: S0014-2999(17)30393-X
DOI: http://dx.doi.org/10.1016/j.ejphar.2017.05.062
Reference: EJP71252

To appear in: *European Journal of Pharmacology*

Received date: 30 July 2016
Revised date: 5 May 2017
Accepted date: 31 May 2017

Cite this article as: Hugo Geerts, Athan Spiros, Patrick Roberts and Robert Carr Towards the virtual human patient. Quantitative Systems Pharmacology in Alzheimer's Disease, *European Journal of Pharmacology* http://dx.doi.org/10.1016/j.ejphar.2017.05.062

Towards the virtual human patient. Quantitative Systems Pharmacology in Alzheimer's Disease.

HUGO GEERTS[1,2], ATHAN SPIROS[1], PATRICK ROBERTS[3], ROBERT CARR[1]

[1]In Silico Biosciences, Lexington, MA

[2]Perelman School of Medicine, Univ. of Pennsylvania, Philadelphia, PA

[3]Department of Biomedical Engineering, Oregon Health & Science University, Portland OR

[*]Corresponding author: In Silico Biosciences, Perelman School of Medicine, Univ. of Pennsylvania. Hugo-Geerts@In-Silico-Biosciences.com

ABSTRACT

Development of successful therapeutic interventions in Central Nervous Systems (CNS) disorders is a daunting challenge with a low success rate. Probable reasons include the lack of translation from preclinical animal models, the individual variability of many pathological processes converging upon the same clinical phenotype, the pharmacodynamical interaction of various comedications and last but not least the complexity of the human brain. This paper argues for a re-engineering of the pharmaceutical CNS Research & Development strategy using ideas focused on advanced computer modeling and simulation from adjacent engineering-based industries. We provide examples that such a Quantitative Systems Pharmacology approach based on computer simulation of biological processes and that combines the best of preclinical research with actual clinical outcomes can enhance translation to the clinical situation. We will expand upon (1) the need to go from Big Data to Smart Data and develop predictive and quantitative algorithms that are actionable for the pharma industry, (2) using this platform as a "knowledge machine" that captures community-wide expertise in an active hypothesis-testing approach, (3) learning from failed clinical trials and (4) the need to go beyond simple linear hypotheses and embrace complex non-linear hypotheses. We will propose a strategy for applying these concepts to the substantial individual variability of AD patient subgroups and the treatment of neuropsychiatric problems in AD. Quantitative Systems Pharmacology is a new 'humanized' tool for supporting drug discovery and development in general and CNS disorders in particular.