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New drug screening strategy for infectious diseases: The power of common sense

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Clinical trials are generally interrupted by poor drug efficacy tested late in the pipeline. By that time, vast amounts of money and resources have been wasted on a product that will not reach the market, which deters investors away from Biotech/Pharma. The current reaction is to reduce R&D teams to focus on pushing potential sources of income out of the pipeline. Alternatively, we propose to improve clinical trial success by using better *in vitro* disease models to "kill" inefficient candidates before they enter complex animal protocols and "metabolites in safety testing" (MIST). The development of drug inhalation therapies for cystic fibrosis (CF) is an example of how common sense will revolutionize drug discovery. The capacity of a compound to improve airway clearance is routinely tested on cultures of human airway epithelial cells. This high-throughput technique has yielded drugs well tolerated in subjects, but which failed to improve airway clearance in CF patients. We demonstrate the critical importance of a screening strategy accounting for the chronic airway infection experienced by most CF patients. Cultures of epithelial cells from CF patients, chronically exposed to their secretions, constitute a more accurate model of the disease, as demonstrated by *in vivo* immunolocalization of protein markers. Surprisingly, this model revealed that the airway walls functionally express a different set of surface proteins, which may affect drug target availability. This study illustrates the tremendous potential of this approach to improve the stringency of drug screening, and the success of clinical trials for infectious diseases.

Biography

Dr. Picher is a medical research scientist specialized on respiratory diseases, with 12 years of experience in drug discovery. As principal investigator at the Cystic Fibrosis/ Pulmonary Research and Treatment Center (NC), she discovered a new signaling pathway regulating airway clearance, currently targeted by Biotech/Pharma. As independent consultant expert for CFRx and Flatley Venture Capital (FVC), she currently provides advices on *in vitro* models and drug screening protocols, and evaluates the scientific soundness of drugs selected for clinical trials by companies soliciting partnership with FVC. Dr. Picher published 75 scientific documents and is editor-in-chief of a book on drug discovery (Springer, 2011).