
Disease Avatars: the epistemology of cell reprogramming-based disease models

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Abstract

Since the landmark derivation of induced pluripotent stem cells (iPSC) from somatic cells in 2006, cell reprogramming has been framed as a revolutionary development not only for the prospects of regenerative medicine but also, and likely in a shorter timeframe, for our capacity to understand human genetic diseases through cellular models. In principle, cell reprogramming makes it possible, for the first time in the history of medicine, to make human genetic variation experimentally tractable through the creation of genetically matched cell lineages on which to decipher and target pathology, biological stand-ins or ‘avatars’ of ourselves, as recently proposed. In this work we present a historical and epistemological analysis of this momentous development in biomedicine, asking how these cellular avatars are reconfiguring the normal and the pathological, and through which resources, both material and conceptual. To this end, we bring into relief the following salient epistemological shifts through a combination of discourse analysis and empirical confrontation with laboratory practices: i) the mutual reclassification of in vivo cell types and in vitro developmental milestones, with the vindication of Canguilhem’s intuition that pathology grounds physiology; ii) the explicit investment of reprogrammed cells with clinical features in a bidirectional flux that conflates research and treatment; and iii) the transition of cellular avatars from representational models to measurement devices of physiopathological differences. This epistemological dissection allows then to explain the innovation of reprogramming-based disease modeling in terms of an iterative biomedical platform in which the patient becomes both a source and a target of extrapolation.

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