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Physiological oxygen measurements in vitro – Schrödinger´s cat in 3D cell biology

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Abstract:

After the development of 3D cell culture methods in the middle of the last century and the plethora of data generated with this culture configuration up to date, it could be shown that a three-dimensional arrangement of cells in most of the cases leads to a more physiological behavior of the generated tissue. However, a major determinant for an organotypic function, namely, the dissolved oxygen concentration in the used in vitro-system, has been neglected in most of the studies. This is due to the fact that the oxygen measurement in the beginning was simply not feasible and, if so, disturbed the measurement and/or the in vitrosystem itself. This is especially true for the meanwhile more widespread use of 3D culture systems. Therefore, the tissues analyzed by these techniques can be considered as the Schrödinger's cat in 3D cell biology. In this perspective paper we will outline how the measurement and, moreover, the regulation of the dissolved oxygen concentration in vitro-3D culture systems could be established at all and how it may be possible to determine the oxygen concentration in organoid cultures and the respiratory capacity via mito stress tests, especially in spheroids in the size range of a few hundred micrometers, under physiological culture conditions, without disturbances or stress induction in the system and in a high-throughput fashion. By this, such systems will help to more efficiently translate tissue engineering approaches into new in vitroplatforms for fundamental and applied research as well as preclinical safety testing and clinical applications.

Keywords: physiological oxygen concentration, in vitro, 3D cell culture, organoid, microcavity sensor arrays, optical O_2 measurements