New technologies for the development of 3D models useful for identifying new biomarkers for the diagnosis of neurodegenerative disorders, including amyotrophic lateral sclerosis (ALS)

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Over the past years, there has been a pressing need for standardized, and simple three-dimensional (3D) tissue models that can accurately support biological and pathological investigations (i.e., drug discovery), an objective that has yet to be fully realized. Indeed, 3D models obtained by different techniques have consistently showed superior performance compared with traditional 2D systems. Nonetheless, creating viable tissue constructs in vitro remains a major bottleneck that prevents these models from reaching their full potential. Although current preclinical models are considered the gold standard, they still suffer from substantial limitations, particularly interspecies differences and reduced confidence in the resulting data. Developing bioengineered human disease models could help close this gap by enabling more reliable approaches. Among the techniques, 3D bioprinting has emerged as a valuable technology for evaluating progress and stage of different diseases, such as Amyotrophic Lateral Sclerosis (ALS). Studies demonstrated cutaneous nerve degeneration can mirror neurodegenerative mechanisms acting at the central nervous system. Even if skin biopsy technique is widely used in clinical practice, the procedure is invasive, requiring multiple patients' tissue removals. Therefore, for the diagnosis and stratification of ALS, a 3D innervated skin model by combining 3D printing and electrospinning was developed. In this presentation, the recent advancements on the use of different naturally derived polymers will be discussed. Furthermore, the different chemical strategies to modify these polymers and to: i) confer a shear thinning behavior for the extrusion-based process and ii) improve the mechanical properties, extending the half-life, will be presented. The overall results showed that the physiologically relevant 3D skin tissue model was able to offer standardized research conditions thus accelerating ALS drug discovery and ALS biomarker identification.

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