



### **3DHumanSpinalCord - Unlocking self-patterning competence to engineer 3D human spinal cord**

Organizers direct formation of the body, releasing morphogens to position tissues and organs. But what organizes the organizers? I aim to harness organizer formation to build self-patterning 3D human spinal cord in vitro.

In developing spinal cord, the floorplate organizer secretes Sonic Hedgehog to direct ventral-dorsal patterning. Prof Tanaka (secondment) discovered how to recapitulate this in vitro: single mouse naïve pluripotent stem cells (PSCs) form neural tube organoids and an early pulse of retinoic acid prompts self-organization of floorplate that drives patterning as in vivo. However, attempts to form cognate human organoids have been unsuccessful. There is a restricted window of competence to initiate floorplate formation, which conventional primed human PSCs are unable to access.

To overcome this, I will combine microenvironment bioengineering with new naïve human iPSCs (Prof Elvassore, host) to recapitulate and study human development from an earlier stage, gaining access to molecular events that may underpin later fate specification and tissue organization. By mechanistic analysis in mouse organoids, I will reveal how competence is instated, how it is closed, and how to prolong or re-instate competence de novo. This knowledge will guide me in unlocking the competent state for human PSCs in vitro, and has implications for activating spinal cord regeneration in vivo. By use of sophisticated engineering technologies pioneered in the Elvassore group, I will control the micro-environment to guide tissue growth and formation, mimicking natural physiology and ensuring reproducibility. By engineering 3D organized human spinal cord in vitro, this project will bridge basic knowledge of critical and inaccessible stages of human development with future biomedical applications. This interdisciplinary training opportunity will build on my doctoral expertise in PSC identity transitions, setting me apart with a strong independent niche for my future career.

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**Department:** Department of Industrial Engineering

**Coordinator:** Università degli Studi di Padova (Italy)

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**Find out more:** <https://cordis.europa.eu/project/id/898970>