Biochemical and structural cues of 3D-printed matrix synergistically direct MSC differentiation for functional sweat gland regeneration

With the support by the National Natural Science Foundation of China, the research team directed by Prof. Fu XiaoBing (付小兵) and associate professor Huang Sha (黄沙) at the Research Center for Tissue Repair and Regeneration affiliated to the Medical Innovation Research Department, PLA General Hospital, recently reported that CTHRC1 and Hmox1 synergistically initiate sweat gland (SG) fate of MSCs, which was published in *Science Advances* (2020, 6: eaaz1094).

SGs play a vital role in thermal regulation, and absent or malfunctioning SGs in a hot environment can lead to hyperthermia, stroke, and even death in mammals. Each SG is a single tube consisting of a functionally distinctive duct and secretory portions. It has low regenerative potential in response to deep dermal injury, which poses a challenge for restitution of lost cells during wound healing. A major obstacle in SG regeneration, similar to the regeneration of most other glandular tissues, is the paucity of viable cells capable of regenerating multiple tissue phenotypes. Several reports have described SG regeneration *in vitro*; however, dynamic morphogenesis was not identified, nor was the overall function of the formed tissues explored.

Their group bioprinted a matrix of SG to direct conversion of MSC into a functional SGs and facilitate SG recovery in mice. By ECM differential protein expression analysis, they identified that CTHRC1 was a critical biochemical regulator of 3D-printed matrix for SG specification. Their findings showed that hmox1 responses to the 3D structure activation were also involved in MSC differentiation. Inhibition and activation assay demonstrated that CTHRC1 and Hmox1 synergistically boosted the SG gene expression profile. In summary, biochemical and structural cues are critical impact of the 3D-printed matrix on MSC fate decision into glandular lineage and functional SG recovery.

These findings indicated the role of 3D-printed matrix cues on cellular behavior and tissue morphogenesis and might help in developing strategies for MSC-based tissue regeneration or directing stem cell lineage specification by 3D bioprinting.

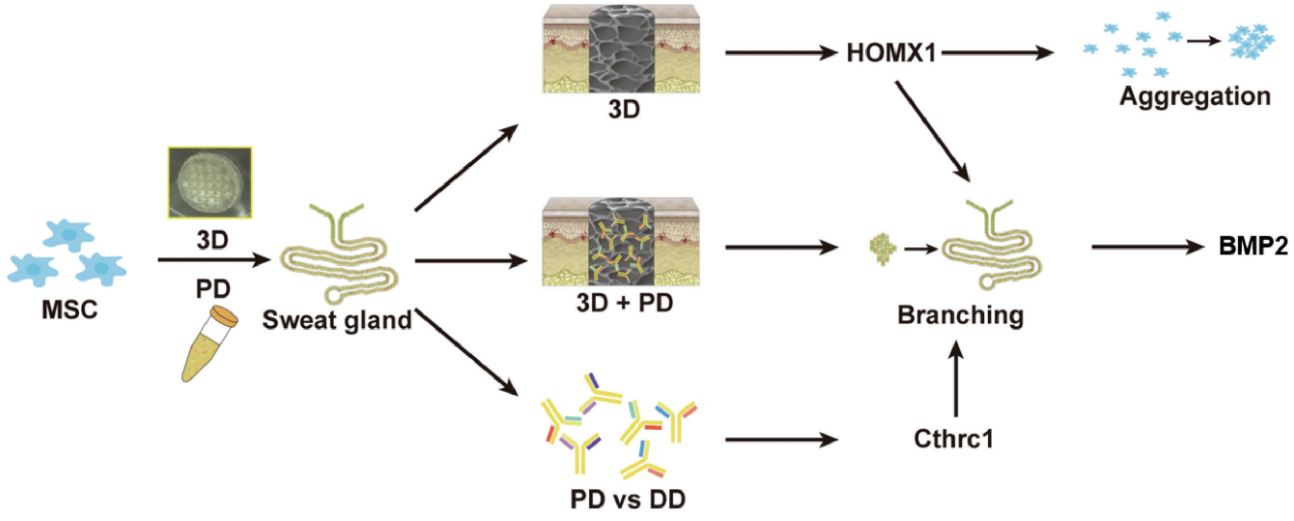

Figure The 3D bioprinted matrix directed MSC differentiation. CTHRC1 and HMOX1 synergistically boost the SG fate of MSC.