Objective

A central question in developmental biology is how the genetic information is differentially interpreted to program cell-fate decisions essential for embryogenesis. The success of developmental cell-fate decisions relies on the accurate rewiring of the proteome to support rapid cellular identity changes. Here, we will address the fundamental question: How is the developmental transcriptome differentially translated in time and space to program cell-fate decisions? I hypothesize that the developmental competence for cell-fate decisions is controlled by fate-specific translational specialization factors (TSFs). TSFs program the selective and privileged translation of developmental genes in defined time windows to enable the
acquisition of cell fate and maintenance of cellular identity. Notably, in a proof-of-principle study, we discovered that translational specialization in pluripotency poises future lineage choices in humans. The research program TRANSCEND has four work packages: (1) identifying candidate TSFs engineering cardiac fate at critical cell-fate transitions by cell-fate specific, systematic cataloging TSFs on ribosomal complexes; (2) dissecting the molecular and functional role of TSFs in cardiac cell-fate specification by combining targeted CRISPR screens and tethered functional approaches; (3) decoding the mechanisms, modalities, and design principles by which TSFs program cardiac identity by using a holistic approach, including loss-of-function studies in cardiac 2D, organoid, and mouse models along with systems-wide methods such as eCLIP-seq and TCP-seq; and (4) engineering translation specialization modules to ameliorate pathological cardiac hypertrophy using patient-derived in vitro and murine in vivo models. Ultimately, the proposed research program TRANSCEND aims at transforming our current understanding of translational control over cell-fate decisions and opening up innovative avenues for controlled therapeutic restoration of cardiac function.

**Fields of science**

natural sciences > biological sciences > biochemistry > biomolecules > proteins > proteomics

natural sciences > biological sciences > developmental biology

**Keywords**

- Cell-fate specification
- regulation of translation
- RNA binding protein
- cardiac development
- gene regulation
- cardiac hypertrophy
- cell-fate decisions
- regulation of cellular identity

**Programme(s)**

HORIZON.1.1 - European Research Council (ERC) - MAIN PROGRAMME

**Topic(s)**

ERC-2021-COG - ERC CONSOLIDATOR GRANTS
Call for proposal

ERC-2021-COG

See other projects for this call

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Coordinator

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Higher or Secondary Education Establishments

Links

Contact the organisation 🔗  Website 🔗  Participation in EU R&I programmes 🔗  HORIZON collaboration network 🔗

Other funding

€ 0,00

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