The evolution of mesoderm and its differentiation into cell types and organ systems

Informe

Información del proyecto

EVOMESODERM

Identificador del acuerdo de subvención: 648861

Sitio web del proyecto

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Proyecto cerrado

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Periodic Reporting for period 5 - EVOMESODERM (The evolution of mesoderm and its differentiation into cell types and organ systems)

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Resumen del contexto y de los objetivos generales del proyecto

Mesoderm, the embryonic germ layer between ectoderm and endoderm, gives rise to major organs within the circulatory and excretory systems and to stabilizing tissues (muscles, bones, connective tissue). We were aiming to study mesoderm development in a variety of animal taxa and trace its differentiation into cell types and organs, with the ultimate aim of reconstructing the history of mesoderm during animal evolution. We describe the morphological and molecular development of mesoderm in these species, and the differentiation of two important mesodermal cell types: nephridia and blood. The results are important, because it helps to understand more about the developmental process, its origin including the origin of human development, organ systems and cell types.

Objectives:

Objective 1: Determining the evolutionary origin of the mesoderm and characterizing the nature of the first mesodermal tissues.

Objective 2: Identifying the changes in developmental programs underlying mesoderm formation that have caused its diversification in different animal lineages.

Objective 3: Tracing the evolutionary differentiation of mesodermal cell types and their organization into novel organ systems.

Trabajo realizado desde el comienzo del proyecto hasta el final del período abarcado por el informe y los principales resultados hasta la fecha

Workpackage 1: Description of the development of target species using advanced imaging technologies and molecular approaches.
During the whole Action we focussed on the description of the development of multiple target species and here with a focus on molecular pathways that are related to mesoderm development. With this project we delivered new insights into the developmental process in all the target species. Further, we included new species which showed mesodermal organ development specifics (e.g. phoronids). One of the major insights came from the description of the processes of gastrulation, the time in embryogenesis, during which the germ layers including the mesoderm are specified. Here we discovered that the behaviour of the site of gastrulation (blastopore) is depending on the processes of axial elongation and mesoderm internalization and does not recapitulate evolutionary ancient processes, as it was proposed by Ernst Haeckel (Martin-Duran et al 2015, Nature Ecology and Evolution). Regarding the late development of mesodermal organs, we studied the nephridiogenesis from a comparative aspect and provided the molecular basis for the homology of all excretory organs that are nephridia like (Gasiorowski et al 2022).

Workpackage 2: Bioinformatic approaches to study genes involved in mesoderm development
During the whole project we studied the gene orthology of mesodermal transcription factors and

signalling pathways throughout the animal kingdom. We applied modern phylogenetic analysis and expanded our studies also to structural genes e.g. in Andrikou et al 2019 PLOS Biology). This challenge we learned to overcome by using advanced orthology assessment, which was successful for most genes. With the emergence of single cell sequencing technologies, we started to early implement these methods. We show that is is essential to incorporate phylogenetic methods in comparative molecular studies (Dunn et al 2018, PNAS) and that care should be taken when homologizing structures based on their molecular underpinnings.

Workpackage 3: Functional studies to test the developmental role of genes using gene knockout and knockdown technologies
Functional studies on non-model organisms are very difficult and this has been proven again in this project. It was one of the high/medium risk elements of EVOMESODERM. However, we performed the inference of signalling pathways using inhibitors in numerous of our studies and were able to dissect the function of e.g. the FGF pathway during mesoderm development in spiralian species. Injection of snRNA, morpholinos were hampered by the fact that some embryos are extremely difficult to inject, even by injection experts.

Workpackage 4. Transgenic animal production
Although we switched to CRISPr Cas9 genome editing from the proposed TALEN techniques, throughout the project it was difficult to establish one species as the major research organism, where the effort to establish the method would have been fruitful. The discoveries made in the other work packages were the main drivers of the studies. In addition, it turned out that in many species mesoderm formation is a very late process from an embryonic perspective, and the transgenesis would infere with earlier processes. In summary, it turned out to be more successful to 1. expand the study to more species and 2. include more pathways for understanding the evolutionary process than to focus on the establishment of transgenesis in 1-2 species.

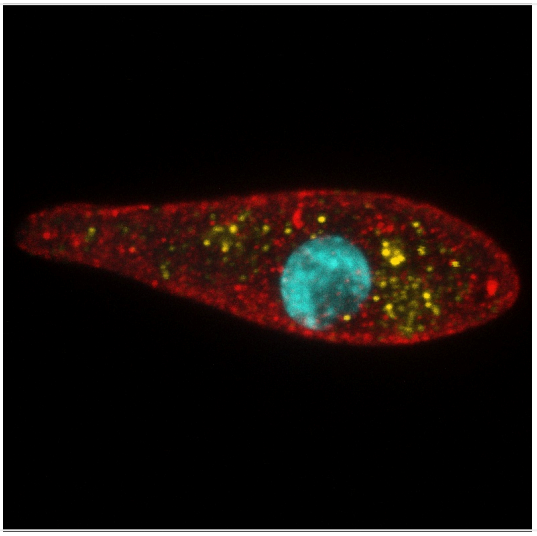
Avances que van más allá del estado de la técnica e impacto potencial esperado (incluida la repercusión socioeconómica y las implicaciones sociales más amplias del proyecto hasta la fecha)

The project EVOMESODERM followed the project planning and described developmental processes and developed new tools. The following breakthroughs can be listed:

Objective 1: “Origins” - Determining the evolutionary origin of the mesoderm and characterizing the nature of the first mesodermal tissues of animals.
We can now say that mesoderm as a layer of cells that are between endoderm and mesoderm is homologous and is driven by similar pathways. The first tissues derived from mesoderm was musculature and gonadal epithelial. These were formed from the same original cell population, which raises the interesting question of the homology of all mesodermal tissues. This raises the question how new cell types evolve. This question is still unsolved and are one of the greatest challenges in biology in single-cell omics times.

Objective 2: “Deviations” - Identifying the changes in developmental programs underlying mesoderm formation that have led to diversification in different animal lineages.
During the course of the project we were able to reconstruct numerous changes in the developmental pathways of mesoderm formation, determination and differentiation. The evolutionary history seems much more variable than expected at the beginning of the project. Even in the so-called conserved transcription factor combinations, that determine cell types, we find deviations (Gasiorowski et al 2022 Current Biology). Alltogether our findings identify molecular replacements, that still do not effect the final outcome as organ. An evolutionary redundancy seems to make sure that the product is formed, although the molecular underpinnings are changing. This result has been also demonstrated by other labs in the recent years for other tissues.

Objective 3: “Novelties” - Tracing the evolutionary diversification of mesodermal cell types and their organization into novel and specialized organ systems.
During our project we showed that for the nephridia (proto- and metanephridia) the molecular underpinnings are e.g. the same (Gasiorowski et al 2022). However, during the evolution of the more complex organs, the morphology has changed quite extensively. This is mainly performed by duplication of existing cells and the inclusion of associated cells from different germ layers. This process is different from our investigation of hemocytes and blood cells. Here, the cells emerge after the mesoderm is formed, and later differentiate into novel, multifunctional cells (see priapulid blood cells). Likely, new cells emerged in each lineage that deviate molecularly extremely, since we could e.g. do not find a homologous cell in other ecdysozoans so far. This is due to the limited amount of published single cell transcriptomic data from other animals.



Blood cell in the priapulid Priapulus caudatus. Staining of actin, nucleus and vesicles.

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