

THE SELF-ENGINEERING OF EMBRYONIC STEM CELLS



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Alfonso Martinez Arias obtained his PhD at the University of Chicago (USA) and is, currently, a Professor of Developmental Mechanics at the University of Cambridge (UK). His main interest is to use interdisciplinary approaches to understand the molecular underpinning of tissues and organs during animal development. After working with *Drosophila* he has dedicated the last few years to establish mammalian Embryonic Stem cells as a model system to study developmental process. Recently he and his group have used engineering approaches to develop 'gastruloids' a new experimental system that allows the recapitulation of early mammalian development in vitro.

How are embryonic stem cells genetically supervised for self-organisation?

The issue is that people, in the organoid field, like to talk about 'self organization' without really understanding the meaning of this term. Physical and chemical systems provide good examples of self organization. The essence of these is that a collection of essentially identical elements, symmetrically distributed break this symmetry spontaneously and, in a non-programmed manner, generate patterns by arranging these elements in space and time: clouds, dunes, snowflakes. Over the last few years it has become clear that stem cells also have an ability to break symmetry from an initial position of symmetry but the difference in this case is that once the symmetry is broken, a program is activated that will determine the patterning processes that follow. This means that although the initial symmetry breaking is spontaneous, the patterning that follows is very much determined (supervised) by the genetic programs that are activated. At the moment we cannot control this supervision but our ability to use stem cells for practical purposes needs our gaining control over it.

How does your work with mice ESCs translate to human research?

At the moment this has not been done but the potential to do this is there.

What do you foresee as the main advancements in self engineering in the future?

The notion of 'self engineering' is, in a way, a different way to express what cells do when they make embryos. There is an engineering process going on but is one that occurs from within, when stem cells make an Intestinal organoid or a mini brain in vitro they are doing it themselves; we hardly intervene. Probably because these in vitro contraptions are isolated, disembodied, and lack a good environment, they are imperfect and, often, not functional. It is here that I think that interactions with engineers will be essential in improving the output of the current organoid 'technology'. Increasing the yield and, importantly, improving the quality of the organoids, making them more like the organs in the organism and capacitating their functionality.

Alfonso delivered a talk for the Stem Cell & Regenerative Medicine Congress.
His talk was titled 'The Self-Engineering Of Embryonic Stem Cells'

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