

Heart in the right place

Symmetry is beautiful but asymmetry has its uses, says S. Ananthanarayanan.

The human body and the bodies of animals have many features of symmetry, but it is their non-symmetric features that make them so efficient and powerful. This asymmetry appears to have arisen in living things in the Cambrian period, some 550 million years ago – a period marked by phenomenal evolution of rudimentary life forms into complex organisms that could later evolve into modern day animals, primates and finally, human beings.

The advantage of asymmetric development is that the organism can specialize, with organs on one side performing one set of functions, while organs on the other side concentrate on another set, instead of repeating the same thing, as they would need to in a symmetric architecture. This is evident in animal bodies, the mouth is at one end and the anus at the other and some organs face one way while the others the other way. Even in the left-right sense, the liver and spleen are on their own sides of the abdomen, the brain is divided into regions on the two sides for different functions and most of all the heart is internally asymmetric and even lies somewhat to the left of centre in the chest. This location of several organs on a particular side is called *situs solitus* and rare cases where the positions are reversed are called *situs inversus*.

The heart

Early in embryonic development, the heart begins to develop into two different halves, one side to drive blood to the lungs and the other to drive blood through the body. This development on one side and not the other is now known to be caused by a set of genes, called *Nodal*, which direct the multiplication of different muscle cells on different sides, to shape the organ for its particular function. Deficiency or errors in *Nodal* is the cause of many congenital heart defects, which affect nearly eight out of a thousand newborns. The heart is extremely sensitive to changes in its normal asymmetry and congenital defects generally imply high rates of disease or mortality. But despite its importance, very little is known about the mechanism of development of organs on one or another side of the body.

Zebrafish

Maria Ines Medeiros de Campos-Baptista from Lisbon and Alexander F. Schier from Harvard, and colleagues recently studied how the *Nodal* family affected the development of heart tissue in real time in the embryo of the *zebrafish*. The zebrafish is a hardy tropical fish, of the minnow family, and a traditional *model organism* in scientific research. The particular advantage for the present study is that embryo of the fish is transparent, which allows internal development to be observed. The development is also rapid, moving from eggs to larvae within three days. Campos-Baptista and Schier used genetically modified zebrafish, which expressed a fluorescent green protein in their heart muscles. The scientists were then able to use a powerful microscope and track how the muscle tissue developed. By controlling the levels of *Nodal* in the specimens, the team found that deficiency in *Nodal* led to slower growth of tissue and particularly to the development of the heart in the centre of the thorax, rather to one side, as is normal.

Zebrafish



This did show that the levels of Nodal were vital. But as viable, although less healthy hearts did develop, it also shows that there are other genes that play important roles in development. The team observes that these other genes need to be identified to fully understand the asymmetric formation of the heart. The information would also illuminate the development of many other internal organs which are vital for life and quality of life.

Situs Inversus

This is a congenital condition where the major internal organs are reversed or mirrored from their normal positions. Thus, in such a person, the liver and gall bladder would be to the left, the stomach and spleen to the right, the blood vessels, the nerves and intestines would go the wrong way round. The heart would also be to the right instead of to the left. But so long as the reversal is complete, it would not be life threatening. In fact, the case of the Ian Fleming character Dr Julius No, who was situs inversus, this saved his life - because his would be killers stabbed him on the left, where a normal man would have his heart!