# Making Faces - Orofacial Evolution, Development and Tissue Regeneration

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'*I never forget a face but can never remember names.*' We are constantly surrounded by faces in the street, in the arts, in the papers. We are bombarded hundreds of times a day each day with new facial images. So why is it so easy for our brains to store and recall such detailed information that allows us to remember individuals faces? Each human face is instantly recognisable as human but each face is unique (Fig 1).

The major sense organs are all collectively located on our faces. We communicate almost entirely with our faces. We feed via our faces. We show all our range of human emotions through changes in our facial features. When faces become disfigured our eyes are naturally drawn to the altered face. Faces are the focal point of human society.

All animal skulls are constructed in the same way involving the same basic organisation of bones and soft tissues. Indeed, the skulls of all vertebrates from fish, frogs crocodiles and man are made of the same basic ground plan of bones and it is the bones that shape the face. Facial features can be reconstructed from the bony skull alone, a property that is increasingly important in forensic science.

What make each skull different are the changes in the form of each of the bones. Fig 2 shows the skulls of two very different species of animals - a turtle and a dog. They are separated by over 150 million years of evolution and, not surprisingly, have very different looking faces.

Fig 3 shows the skulls of two animals of the same species (dogs), which have very different facial forms. These faces have become so different because they have been subjected to very stringent selection via breeding. This illustrates the point that although facial characteristics are conserved, large changes can be produced

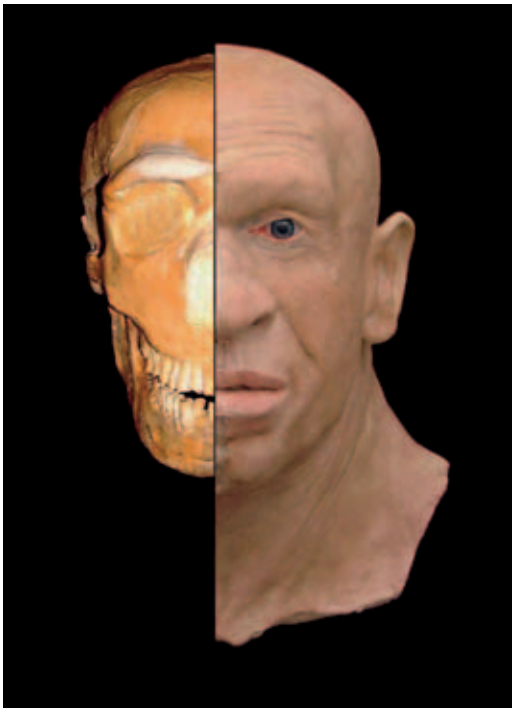

**Fig 1** 3D facial reconstruction from of a Neanderthal from a reconstructed skull. Courtesy of Richard Neave, RN-DS Partnership.

**Fig 2** (top) Left, skull of a turtle. Right, skull of a dog.

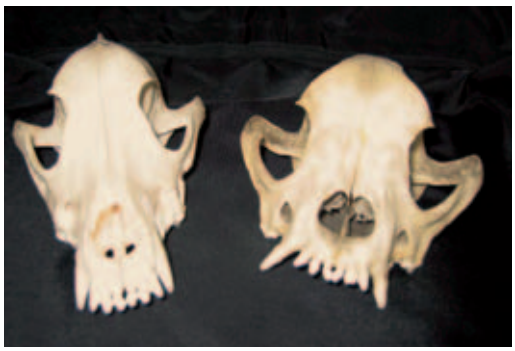

**Fig 3** (bottom) Left, skull of a border collie dog. Right, skull of a boxer dog.

within a few generations of selective breeding. The facial ground plan is rigid by the morphological features that are highly variable. Although progress is slowly being made using the enormous variation in facial form of dogs to identify key processes controlling facial development, more rapid process is being made using modern genetic approaches in the most common experimental systems mainly fish, birds, mice and man (Fondon and Garner, 2004). Since the basic ground plan of craniofacial structure is the same in all vertebrates, each of these different species can be exploited to take advantage of the unique experimental systems:

- Fish - transparent embryos, rapid breeding large-scale mutagenesis.
- Birds - highly accessible embryos for manipulation.
- Mice - targeted genetics
- Man - natural genetics

As more progress is made towards understanding the genetic processes that control this basic ground plan, the basis for the differences in form (morphology) has started to emerge, providing the first clues to what makes faces individual. Presentations in this section where selected to illustrate how studies of different species can reveal the nature of how faces are made and how all this information is coming together to provide real and significant insights into what makes faces. A key question that has emerged over the last few years has been the extent to which this understanding of craniofacial development can be used to develop biological approaches to repair and restore damaged tissues. Central to these ideas is the use and manipulation of stem cells as a way of producing the different cell types and morphology of facial structures.

Bjorn Olsen and Mike Dixon both use the natural resource of human genetics (syndromes) to first identify genes causing human craniofacial malformations and then use targeted mice genetics to re-create these deformities in experimental animals. Bjorn has particularly focussed on bone formation and among his many discoveries was the identification of the gene causing Cherubism (Ueki et al, 2001). Mike's interests include cleft palate genetics and Treacher Collins syndrome for which he identified the causative gene, *TREACLE* (Treacher Collins Collaborative Group, 1996). Ann Husseyune is a evolutionary developmental biologist who has a particular interest in understanding the mechanisms that lead to replacement teeth in animals. Ann, using the zebrafish as a model system, has identified the possible roles of stem cells in producing continuous tooth replacement (Huysseune and Thesleff, 2004). Pam Robey is a bone cell biologist who has pioneered the characterisation of mesenchymal stem cells that can form various hard tissue cells such as osteoblasts. More recently she has been involved in pioneering studies identifying stem cells from different compartments within teeth (Miura et al, 2003). The basic question proposed by Pam's work is whether these different stem cell populations can be used in clinical situations for hard tissue repair. Last but not least, Jill Helms is a developmental biologist who uses the chick embryo as her model experimental system. Jill's research (not published here) has provided a number of fundamental observations on the understanding of facial development, in particular the role of developing brain in shaping the face (Hu et al, 2003). This is a particular interesting observation in light of emerging studies linking facial asymmetries with schizophrenia. Is it possible that facial features reflect brain function? (Hennessy et al, 2004). If so, is this the result of the very close links between early brain and face development in the embryo? If this is so, will disorders such as schizophrenia be diagnosable early in life from facial scans?

Understanding how the embryos make faces is fundamental biological research. Its importance and significance are for more wide-ranging and lie at the very centre of human behaviour.

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