ligaments.

If small chunks of embryonic muscle tissue (consisting of muscle cells mingled with fibroblasts) are also placed in the dish, they become connected to the cartilage rudiments and to one another by bands of collagen equivalent to tendons; the muscle fragments, initially shapeless blobs in random positions, become stretched out into well-formed muscle bellies and are towed into place by the collagenous attachments to the skeleton[5]. Paradoxically, the muscle cells appear to be the passengers rather than the engines of such movements. In an embryonic limb bud that has been deprived of cells capable of developing into muscle, the skeleton at first forms normally, and so do the tendons, even though they have no muscles to pull on them[11].

Oriented fibrils in an extracellular matrix can orient cell movements (as a paper in this issue of *Nature*, p.453, from Norio Nakatsuji and K. Johnson demonstrates in the context of the amphibian gastrula[12]). When fragments of tissue are explanted into a collagen gel, cells — presumably fibroblasts — migrate out into the uninhabited regions of the gel; and the migrants move most rapidly, and in largest numbers, along the dense oriented bands of collagen that have been created by fibroblast traction. Thus the fibroblasts govern the disposition of collagen, and the collagen in turn affects the disposition of the fibroblasts.

Furthermore, a strong and active cluster of fibroblasts surrounded by collagenous matrix will tug towards itself not only the matrix but also any fibroblasts that may be clinging to it. Once recruited into the cluster, these cells will add to its strength. Thus inhomogeneities in the distribution of fibroblasts will tend to be self-amplifying.

Clearly, fibroblasts and collagen fibres together make a most remarkable dynamic system. A recent paper defines its properties in mathematical terms and discusses its capabilities for pattern formation[13]. For example, a homogeneous tissue of fibroblasts dispersed in a random matrix may become unstable against small departures from uniformity, and so spontaneously develop a pattern in which the cells become clustered and the collagen becomes organized into tracts.

Just such a phenomenon is seen in the skin of a bird embryo as feather tracts form. The fibroblasts of the previously almost uniform embryonic dermis gather into a regular lattice of condensations, corresponding to feather rudiments, linked by oriented bands of collagen. The whole transformation is blocked in the presence of collagenase[14]. In appropriate conditions, an artificial gel of collagen containing dispersed fibroblasts will show roughly similar behaviour[15,16]. Theory and experiment here converge in a most persuasive way.

A bolder and more dubious application of the theory of fibroblast traction aims to explain the origins of the pattern of long bones in a developing limb as a result of mechanical instabilities in the mesenchyme of the undifferentiated limb bud, creating non-uniformities where none existed before[13]. Limb-bud specialists are likely to be sceptical: there is too much evidence that cells of the apparently undifferentiated mesenchyme are already intrinsically different and determined for the formation of specific skeletal structures even before any cartilage 'condensations' are visible[1]; and the patterning of the skeleton seems too insensitive to artificial and mechanical disturbances. There is surely more to pattern formation in the developing limb than mechanical instabilities generated by fibroblast traction: but it is no less sure that fibroblast traction plays a major part in the process. □

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Obituary

Ahmad Bukhari 1943–1983

from Neville Symonds

AHMAD BUKHARI had exercised a formative influence on research in transposable elements for close to a decade and was at the height of his powers when he died suddenly of a heart attack on 19 November 1983.

His earliest major contribution, in 1975, concerned the excision of transposable elements, an issue he always felt was undervalued in the rush to understand how replicative transposition occurs. He was able to show that most bacteriophage Mu insertions in a host gene could be excised exactly with the restoration of gene activity, so demonstrating for the first time that Mu transposition normally occurs without any damage to target DNA sequences.

With regard to replicative transposition, he and Ljungquist published a crucial paper in 1977 showing that coupled transposition and replication of Mu proceeds without Mu leaving its original prophage site. Using an ingenious combination of restriction analysis and DNA–DNA hybridization, they examined the state of prophage Mu DNA after induction and were able to demonstrate conclusively that the original Mu-host junction fragments remained intact well into the latent period after many rounds of replication had occurred.

Bukhari's strength as a scientist rested on his ability to see problems as a whole and to appreciate the elements that were crucial to their understanding. This is exemplified in the beautiful review he wrote for *Annual Review of Genetics* (**10**, 389) in 1976, 'Bacteriophage Mu as a transposition element', in which he brought together the known experimental findings about Mu, assessed their importance from the viewpoint of transposition, indicated the areas where further ideas and investigations were needed and finally related Mu behaviour to that of other insertion elements.

Recently, research on Mu at Cold Spring Harbor has focused on the mechanism by which Mu transposes, paying particular attention to the findings that transposition sometimes leads to replicon-fusions (alternatively called co-integrates) and sometimes to simple insertions. These studies led Harshey and Bukhari to propose a variant to the Shapiro model for transposition which has stimulated a considerable amount of theoretical discussion and practical activity, and which is supported by observation of Mu transposition intermediates using electron microscopy.

Bukhari was born in the Punjab and was an undergraduate at the University of Karachi, leaving for the US in 1966 to carry out graduate studies at Brown University and the University of Colorado. From 1970 he worked continuously at the Cold Spring Harbor Laboratory, and was the centre of one of the most active research groups working with bacteriophage Mu.

As a person Bukhari was emotional and enthusiastic with a variety of interests and friends. He maintained his connections with Pakistan, at the personal as well as the scientific level, and was a scientific adviser to both UNESCO and UNIDO. He will be sorely missed both for his intuition as a scientist and for his humanity as a friend. □

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