Previously unpublished paper by Francis Crick and Jeffries Wyman, "A footnote on allostery"

April 18 2013

It is rare that an unpublished piece of research or theory remains significant after half a century. It is also a wonderful example of the boundless curiosity of the late Francis Crick. A previously unpublished work by Francis Crick and Jeffries Wyman from 1965 is now available, together with Jean-Pierre Changeux's recollections on the origins of the theory of Allostery and several important texts by various authors on the subject. These are part of a special issue of the *Journal of Molecular Biology* (*JMB*) published at the occasion of a Pasteur/EMBO Conference on Allosteric Interactions in Cell Signaling and Regulation to be held at the Pasteur Institute in Paris, May 14-17, 2013, to mark a half-century of research on this subject.

Early in 1963 an influential theory was published by Jacques Monod, Jean-Pierre Changeux and François Jacob in JMB to explain how binding of a regulatory molecule could influence the binding of a completely different kind of molecule at topographically distinct sites. The word allosteric was invented, based on the Greek allos "other", and stereos "solid (object)" and a conformational change postulated to account for the interaction between sites. The theory was further extended in 1965 by Monod, Wyman and Changeux in a classical paper dealing in particular with the important threshold effects that accompany the binding of ligand molecules to regulatory proteins and that they assigned to the cooperative multi-subunit organization of the protein. One issue of the theory related to how the conformational transition

involved in the signal transduction process was influenced by the number of sites for each ligand. The Crick-Wyman manuscript proposes a somewhat different formulation of Monod-Wyman-Changeux hypothesis through the critical analysis of how the regulatory performances of a monomeric protein are enhanced by their assembly into a cooperative structure.

An initial version of the manuscript was initially circulated within Jacques Monod's group at the Pasteur Institute, but the text was never submitted for publication. Stuart Edelstein, an Editor of the special issue, arranged posthumous publication and has written a preface to place the text in context.

Francis Crick had a strong impact in several areas of biology, but most scientists will be surprised to discover that he also took a strong interest in allosteric interactions. A major research institute bearing his name is currently under construction in Central London. Sir Paul Nurse, Chief Executive of the new institute and President of the Royal Society commented on publication of the Crick-Wyman text: "As we enter into the final phases of construction of the Francis Crick Institute, it is satisfying to discover yet another feather in Francis Crick's already crowded cap. Few knew that he took a serious interest in allosteric proteins and developed original ideas that after nearly fifty years still remain relevant to current research issues. Bringing this unpublished text to the scientific community is an exciting event to mark the 50th anniversary of allostery."

The conference in May at the Pasteur Institute will include presentations by 40 world-renown scientists, including seven Nobel Prize laureates. The program comprises seven half-day sessions devoted to various subjects for which allosteric interactions play an important role, including enzymes, receptors, chaperones, ribo-switches, and complex molecular machines such as ribosomes, motors and replication

complexes.

An exhibition shall be presented at the Pasteur Institute during the conference on the history of allostery and subsequent debates based upon original documents selected by Henri Buc from the Pasteur Institute's archives.

Francis Crick (1916-2004) was awarded the Nobel Prize for Physiology or Medicine in 1962 along with James Watson and Maurice Wilkins for their work in describing the structure of DNA and its significance for information transfer in living things. Jeffries Wyman (1901-1995), a distinguished physical chemist of proteins was a founder and past secretary general of the European Molecular Biology Organization (EMBO). Jean-Pierre Changeux completed his PhD with Jacques Monod on the bacterial regulatory enzyme, l-threonine deaminase, leading to the discovery of "allosteric" sites. He subsequently isolated the nicotinic acetylcholine receptor and demonstrated its allosteric properties. Changeux, a member of the National Academy of Sciences (USA), has received the Wolf and the Balzan prizes, and is currently Honorary Professor at the College de France and the Pasteur Institute.

More information: The articles are "A Footnote on Allostery" by F.H.C. Crick and Jeffries Wyman (dx.doi.org/10.1016/j.jmb.2013.03.012), and "The origins of allostery: From personal memories to material for the future" by Jean-Pierre Changeux (dx.doi.org/10.1016/j.jmb.2013.02.033). The articles appear in The *Journal of Molecular Biology*, Volume 425, Issue 9, pages 1500-1508 and pages 1396-1406, respectively, (May 13, 2013)

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