LECTURES

FROM AN INTEGRIN BINDING PROTEIN TO AN EVOLUTIONARILY CONSERVED TRANSLATION FACTOR NECESSARY FOR THE CONTROL OF METABOLISM

S. Biffo

Laboratory of Molecular Histology and Cell Growth, INGM, and Department of Biosciences, University of Milan, Italy

E-mail: stefano.biffo@unimi.it

eIF6 (alias p27BBP, Beta4 Binding Protein) was cloned for its capability to bind Beta4 integrin. Rapidly, we learned that it is a factor necessary for ribosome biogenesis and translation,[1] highly expressed in embryonic and cancer cells. eIF6 is rate-limiting for translation under growth factors and oncogenic signaling.[2] eIF6 acts by regulating at the translational level the metabolism of fatty acids.[3] In general, eIF6 reduction increases animal fitness, resistance to tumors and to high fat diet. Why are then high levels of eIF6 maintained *in vivo*? We find that high levels of eIF6 are essential in the immune system. In conclusion, we speculate that translational control acts as a form of "metabolic learning".

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THEORIA GENERATIONIS: THE ANCIENT ROOTS OF THE MODERN DEVELOPMENTAL BIOLOGY

E. Capanna

Department of Biology and Biotecnologies "C. Darwin", Sapienza University of Rome, Italy

E-mail: ernesto.capanna@uniroma1.it

Metaphysical concepts are present in Greeks pre-Socratic Philosophy that will form, until present days, the Ariadne thread of the analysis of developmental processes. The debate between *to be* and *to become*, that opposed Parmenides *vs* Heraclitus, along the two subsequent millenniums, will turn to the dilemma between preformation *vs* epigenesist, immanence *vs* transcendence. Aristoteles was the first to transfer the question from Metaphysics to Physics enunciating the *Theoria generationis*. In the Hellenistic period, and during the Renaissance, the autopsy and experimental methods became key to the interpretation of biological processes. The crisis of the Aristotelism was already in place following the studies of Italian anatomists, but the final trespass was due to William Harvey in his *De motu cordis*. Harvey was author of a second work: in his *Exercitatione de generatione animalium* he introduced, with his aphorism *omne vivum ex ovo*, the concept of *ovism*. In the same years, the description of the spermatozoon (*animalculum*) was formed, and Harvey's ovism and animalculism became counterparts. Both theories were to be read according to preformation and epigenetic approach. With the Enlightenment the dispute over the development process was placed in the Cartesian rationalism, and subjected to rigorous testing. Excels among others the figure of Lazzaro Spallanzani. The positivism of Comte moved to search the material *prime causes* of the development, according the laws of Physic and Chemistry. During this period come the experiences on *prelocalization* of embryonic areas of Carl Vogt, and the *mosaic egg* of Roux with clear immanent evidence. A finalistic interpretation reemerged from experiences of Driesh concerning the *embryonic regulation*, and from those of Spemann on *embryonic induction*: the morphogenesis was conceived as a dialectical process between inductive power of the organizer and the specificity of the morphogenetic fields. In the middle of last century two notes on Nature by Crick and Watson were published: the millenary fight between preformation and epigenesist was finally solved: the development program is preformed in the genome, but varied in epigenetic interactions between parts of the genome itself, and with the cell environment in which the genome operates.

SEA URCHIN RESEARCH: MILESTONES, MEMORIES, AND FUTURE CHALLENGES

V. Cavalieri

Department of Biological, Chemical and Pharmaceutical Sciences and Technologies, University of Palermo, Italy

E-mail: vincenzo.cavalieri@unipa.it

The sea urchin eggs and embryos have been used for nearly two centuries as experimental models for classical and modern developmental biology. In the late 1870s, the ground-breaking observations independently obtained by Hertwig and Fol highlighted for the first time that a single sperm enters the oocyte and the male and female pronuclei fuse at fertilization.[1] From that point on, the seminal studies of Boveri, Driesch, and Herbst allowed conceptualization of basic biological themes, such as the chromosome theory of heredity.[2] In the first half of the twentieth century, the embryo manipulation experiments performed by Hörstadius and Runnström further advanced the field, introducing the concept of morphogens double gradient.[3] Later on, with the flowering of molecular biology and the advent of new technologies, scientists of the caliber of Hultin, Monroy, and Davidson emphasized that this echinoderm also represents an excellent model for studying the molecular basis of embryogenesis.[2] In the post-genomic era, the sea urchin embryo continued to be an unsurpassed model for determining the molecular mechanisms responsible for creating a multicellular organism, mainly because of its relative inexpensiveness, optical transparency, rapid synchronous development, and amenability to perform a powerful arsenal of experimental procedures.[4] Although nowadays the carrying capacity is much lower than in years past, the sea urchin embryo is still a convenient model to study gene regulatory networks,[5] response to environmental stressors,[6] biomineralization,[7] stem cell properties,[8] and cancer.[9] Undoubtedly, the breath of all this research makes it clear that the sea urchin embryo could help further generations of investigators to reveal the unsolved mysteries of life.

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