Editorial

A new step in drawing a biomolecular guide for developing cells

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Treating cancer is an illustrative example on why the understanding of fundamental biological processes one of the most fundamental challenges in life sciences. Major leaps have already been made on the genetic and biological basis of this disorder. Using massive parallel techniques like gene expression arrays have given us elaborate descriptions of the differences between, organs, healthy and diseased tissue and other models. Unfortunately, these descriptive approaches have yet to provide us with a clear explanation on how the biology of the cell is organized. Nevertheless many epiphanic glimpses into the organization of biological mechanisms have been published revealing a stunning complexity based on simple instructions. One such significant insight was the link between embryogenesis and cancer (1). Since then many groups have elaborated on this landmark observation and nowadays it is commonly accepted that embryological important patterning mechanisms are at the basis of deregulating "properly aware" cells to develop a niche for uncontrolled growth and eventually tumors. The analogies between the embryological processes and tumor development further enabled researchers to use the strengths of each model to increase our understanding of tumorigenesis. Nowadays the role of defective wnt, hedgehog, SMAD and Notch signaling in tumors in gastric tumors has been found (2). However, to fully appreciate the complexity of the biology behind this model, it is essential to take into account several aspects of the players in this process. At multiple levels of cell communication, several factors are at interplay between each other in a spatiotemporal manner. With these premises, cells are presented with a biomolecular guide which tells them for example, where they are and what they are supposed to do. This notion can be expanded with the hypothesis that changes in the biomolecular guide could result in altered responses but more often in non-sense resulting in premature apoptosis. Nevertheless, different elements in this biomolecular guide are needed to draw a readable map. Removing or adding one compound could therefore result in no, small or dramatic changes in readability. This analogy shows the intricately linked roles of different signaling mechanisms in cell physiology.

The article by Sartori da Silva *et al*. in this issue of Translational Gastrointestinal Cancer further expands on this idea (3). The authors elaborate using earlier data in which they have shown the importance of d-Asb11 (ankyrin and SOCS-box containing protein) in the assembly of the biomolecular guide during development. d-Asb11 was shown to be of great importance in the regulation of compartment size (4-6). By using the developmental model of the zebrafish they showed that d-Asb11 has a critical role in (re)setting boundaries through interference with the delta/notch signaling gradient. When d-Asb11 is present, cells are not able to set a Delta/Notch gradient resulting in postponed differentiation and thus enabling cells to increase the size of the compartment in which it is expressed. This effect has already been observed in the neuronal and muscle compartment of the zebrafish and in this issue the potential has been expanded to the mammalian gastrointestinal domain (4-7). The authors explain the evolutionary background of d-Asb11 and its human homologues, showing common ancestry and a possible gene duplication process of ASB9 and 11. Next, they provide data in which co-expression of d-Asb11 and gastrointestinal markers indicate a potential common developmental links. Subsequently, they show that ASB9 is most probably the human candidate for the previously reported d-Asb11

function in the gastrointestinal system. The authors conclude with a possible functional link of ASB9 to cancer when they compare the expression of ASB5, 9, 11 and 13 in normal and adenoma tissue and see increased expression of ASB9 in adenoma, which is in agreement with previous work published by Tokuoka *et al*. (8).

Sartori da Silva *et al*. show in this paper that ankyrin and SOCS-box containing proteins have the potential to be important factors in the development of multiple organs in an embryo, further strengthening the role of controlling compartment size in cell physiology.

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