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EDITORIAL

Destroy to create

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"It is always a matter of using the same elements, of adjusting them, of altering here or there, of arranging various combinations to produce new objects of increasing complexity. It is always a matter of tinkering." In his provocative and deep interpretation of evolution and development in particular, and life in general, Jacob (1977) stressed the point that biological novelty is created when pre-existing sub-systems are combined into a new and often different context. Implicitly to this view, these sub-systems have to be displaced out from their previous context. Following this rationale, destruction is the prerequisite of creation. However, while the rules and principles leading to the organisation of a new system have attracted considerable attention, our understanding of the rules and principles that govern the regulated disintegration of a system, lags far behind. Sure, there has been growing interest in apoptosis and programmed cell death for their medical and applied relevance. However, it is often neglected that these phenomena represent just one of the many facets of a larger biological principle. Biological systems are dismantled in an ordered fashion, such that their elements become accessible for future "tinkering". Three contributions in the current issue highlight different aspects of controlled cellular destruction.

That dismantling extends beyond mere cellular suicide becomes already clear from the first contribution by Klemencic and Funk (2017) in the current issue that review comprehensively the non-metazoan caspase homologues. The discovery of orthocaspases in cyanobacteria and the identification of metacaspases in microalgae was first surprising, because a cellular suicide does not make sense in a situation of "egoistic" cells that mutually compete. This has later been remedied by considering the algal population as a whole, where the self-sacrifice of some cell for genetically identical or at least closely related cells can be understood as selective advantage (a kind of microbial kin-selection theory). However, the main point of this review is to highlight the structural and functional overlaps and specificities between caspases and their non-metazoan homologues. While ortho- and metacaspases share structural features of the central domain, they not only differ with respect to their substrate specificity, but also with respect to their regulatory patterns. Some of them are expressed in the context of specific developmental events or even constitutively, which is not that what one would expect from a molecule acting in cellular suicide. Authors warn from precocious conclusions on the function of these homologues just based on assays with artificial substrate kits. So, some of the non-metazoan caspases might be tools of dismantling, but not necessarily executors of programmed cell death.

The strong interest in apoptosis is mainly driven by medical application. The ability of cancer cells to evade the signals activating apoptotic removal of damaged cells has become a major focus in medical cell biology. For instance, leukemic cells lacking the control protein p53 show unrestrained entry into DNA synthesis, such that the only remaining checkpoint to restrain their proliferation is the transition from G2 to mitosis. In their contribution, Lakshmipriya et al. (2017), in the current issue, use extracts from a plant employed in traditional Ayurvedic medicine to selectively induce DNA damage in a leukemic cell line such that the quality check at the entry of mitosis is activated leading to a mitotic catastrophe, inducing, among others, the caspase pathway. Since normal lymphocytes do not respond to this extract, there is potential to develop a specific therapy.

Also the third contribution, by Zhou et al. (2017), in the current issue, deals with a therapeutic activation of cellular dismantling, so called systemic programmed cell death. This phenomenon can be observed in root tips of Solanacean plants that have been infected by the Tobacco Mosaic Virus. This virus can travel from cell to cell hijacking the cytoskeleton of its host targeting the viral RNA to the plasmodesmata. Authors show that root tips that do not contain viral particles themselves, nevertheless are dismantled by an autophagosomal pathway as described previously for the tapetum, the cell layer developing and later feeding the pollen

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(Papini et al. 2014). This means that the controlled dismantling of a cell can be triggered by signals coming from other cells, thus preparing an adaptive response before the cell itself has made contact with the pathogen.

These three examples not only illustrate the variability in functional context, where cells are dismantled, it also shifts to the focus from the question, **whether** cells are eliminated by apoptosis or programmed cell death to the manner, **how** this dismantling happens. This **how** may depend on that what afterwards is supposed to be created from the dismantled components. Cell death, thus, turns into a central tool of "Nature as Tinkerer".

Compliance with ethical standards

Conflict of interest The author declares that he has no conflict of interest.

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