FBS Seminar

August 11 (Tue), 2015
16:00 - 17:00

3F Seminar room, Nano-biology Bldg

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Novel activation mechanism of the macromolecular complex APC/C ubiquitin ligase

高分子タンパク質複合体 APC/C ユビキチンリガーゼの新たな制御機構

Proteolysis is the breakdown of proteins into amino acids, which is an essential process not only providing building blocks for new protein synthesis but also allowing cell and tissue regeneration and degradation of damaged and regulatory proteins during cell division, transcription, signal transduction and the immune response. This proteolysis must be selective and is achieved by tagging the target protein with a small molecule called ubiquitin. Over 700 genes in our body are involved in ubiquitin-mediated proteolysis and misregulation of proteolytic control can lead to cancer, metabolic syndromes, neurodegenerative disease and ageing.

In our laboratory we study one of the key cellular enzymes involved in this ubiquitin-mediated proteolysis, the anaphase-promoting complex/cyclosome (APC/C). This enzyme controls genome DNA duplication and distribution to daughter cells as well as cell growth, differentiation and death. In addition, the APC/C modulates DNA damage repair, brain function and metabolic processes. As such, a better understanding of how the APC/C works in cells is of benefit for human health providing the possibility of discovering potential biomarkers for early diagnosis of disease and valuable information useful for the development of new drugs.

To fully understand the biological function of the APC/C in health and disease and to develop therapy, new drugs or possible interventions, it is imperative to study the APC/C-ubiquitin system in its entirety, from the cellular down to the molecular level. In the past, the individual role of vertebrate APC/C subunits and their regulation has been believed to be extremely difficult to dissect due to the complexity of the subunits (over 13 subunits, 1.5 MDa complex). In fact, it was impossible to reconstitute apo-APC/C until recently. However, our latest development APC/C re-constitution using the MultiBac system will enable us to manipulate APC/C function at will and together with the Xenopus egg system, detailed analysis of vertebrate APC/Cs can be achieved to a level never attained before. We are on the verge of discovering a most critical step by which APC/C co-activator Cdc20 is allowed to interact and activate the APC/C ubiquitin ligase via its N-terminal conserved motif. We will discuss the mechanisms of action and regulation of the APC/C ubiquitin ligase with our latest data.

Chairperson: Tatsuo Fukagawa