2SAA-01 ミトコンドリアと抗 RNA ウイルス自然免疫**Mitochondria and antiviral innate immunity in mammals****Takumi Koshiba** (*Dep. of Biol., Faculty of Sci., Kyushu Univ.*)

Mitochondria, cellular powerhouses of eukaryotes, that undergo cycles of homotypic fusion and fission events are recently known to act as a central hub for cellular innate antiviral immunity in vertebrates, particularly mammals. Because mitochondria are believed to have evolved from organisms such as alpha-proteobacterium, their newly discovered role of branching into the host-cell defense was unexpected. In this meeting, the recent insights into the fundamental phenomenon of mitochondrial involvement in cellular innate antiviral immunity will be discussed.

2SAA-04 オートファジーが駆動するミトコンドリア分解の仕組み**Targeting Autophagy for Mitochondrial Clearance****Koji Okamoto** (*Grad. Sch. Frontier Biosci., Osaka Univ.*)

Mitophagy in yeast requires Atg32, a transmembrane protein anchored on the surface of mitochondria. Atg32 interacts with Atg8, a phosphatidylethanolamine (PE)-conjugated ubiquitin-like protein localized to autophagosomes. Recently, we found that mitophagy is strongly impaired in cells lacking Opi3, a phospholipid methyltransferase acting in conversion of PE to phosphatidylcholine. Strikingly, the levels of lipidated Atg8 were drastically increased in the absence of Opi3. Atg8 is conjugated to phosphatidylmonomethylethanolamine (PME) in the opi3 mutant. In vitro, Atg8-PME is not efficiently delipidated by Atg4, a cysteine protease essential for autophagy. Our data suggest that the regulation of Atg8 lipidation and recycling is critical for mitophagy.

2SAA-02 カルシニューリンと Notch シグナリングを介してミトコンドリアの融合は心筋細胞の分化に必須である**Mitochondrial fusion controls differentiation of ESCs into cardiac cells via a novel pathway of calcineurin and Notch signaling****Atsuko Kasahara**¹, Luca Scorrano² (¹*University of Geneva, CMU,* ²*University of Padua, Dep. of Biology*)

Mitochondrial fusion-deficient mouse embryonic stem cells (ESCs) revealed altered subcellular mitochondrial distribution results in increased capacitative Ca²⁺ entry and calcineurin activity, and impaired cardiac differentiation. These changes caused increased nuclear NICD1 level, suggesting Notch1 activation. A pharmacological rise in intracellular Ca²⁺ level by ionomycin fully recapitulated the calcineurin dependent activation of Notch1, and inhibition of calcineurin normalizes Notch1 activity and rescues the cardiac differentiation in fusion-deficient ESCs. Mitochondrial shape and localization impact nuclear programs of differentiation through previously unexplored interconnected signaling pathways via Ca²⁺, calcineurin and canonical Notch signaling.

2SAA-05 酵母ミトコンドリアにおけるタンパク質と脂質の輸送機構**Mechanisms of protein and lipid transport in yeast mitochondria****Toshiya Endo** (*Fac. Life Sci., Kyoto Sangyo Univ.*)

Mitochondrial biogenesis requires synthesis and transport of its constituent proteins and lipids. Most mitochondrial proteins are synthesized outside mitochondria and subsequently imported into mitochondria. We have recently identified a new pathway for import and sorting of N-anchor mitochondrial outer membrane proteins, which unusually requires both the protein translocators in the outer and inner membranes. Mitochondrial phospholipids are synthesized by multiple phospholipid-synthetic enzymes located in different organelles including the endoplasmic reticulum (ER) and mitochondria. I will discuss our latest results on the structural basis for the possible lipid transport between ER and mitochondrial membranes.

2SAA-03 ミトコンドリア呼吸鎖の多様性：寄生虫からがん細胞まで
Diversity of mitochondrial respiratory chain from parasite to cancer**Kiyoshi Kita** (*Dept of Biomedical Chemistry, Graduate School of Medicine, The University of Tokyo*)

Starvation of glucose and hypoxia are observed in hypovascular tumors pancreatic cancer. Increased glycolysis is the principal explanation how cancer generates energy in hypoxia, but under such condition, glycolysis alone cannot explain how cancer cells maintain their required energy levels. To understand energy metabolism in tumor cells under the tumor microenvironment, we have been focusing on the mitochondrial energy metabolism, NADH-fumarate reductase system found in anaerobic organisms such as parasitic helminthes, such as *Ascaris suum*. Thus, NADH-fumarate reductase system is important in maintaining mitochondrial energy metabolism of many parasites under hypoxic conditions and the tumor microenvironment, and is a novel target of anti-cancer therapy.

2SBA-01 電子顕微鏡法により示された線虫イネキシン 6 ギャップ結合チャネルの特徴的なサブユニット構成**Electron microscopy of *C. elegans* innexin-6 gap junction channels indicates a characteristic subunit organization****Atsunori Oshima**¹, Tomohiro Matsuzawa², Kazuyoshi Murata³, Kouki Nishikawa¹, Yoshinori Fujiyoshi¹ (¹*CeSPI, Nagoya Univ.*, ²*Dept. of Biophys., Grad. Sch. Sci., Kyoto Univ.*, ³*NIPS*)

Innexin is a molecular component of invertebrate gap junctions. The 3D structure, however, remains unknown. Here we performed an electron microscopic analysis of solubilized, reconstituted, and 2D crystallized *C. elegans* innexin-6 (INX-6) gap junction channels. Cryo-electron microscopy and single particle analysis of purified INX-6 channels revealed class averages with eight rotational peaks. 2D crystals of INX-6 channels were generated in a hexagonal lattice, and image processing revealed a projection map that clearly demonstrated eight separated densities around the pore. These findings suggest that the subunit number of INX-6 channels is distinct from that of vertebrate connexin channels, which contain 12 subunits in a full gap junction channel.