＜2021年度９月期　生命機能研究科中間評価論文公聴会について＞

生命機能研究科では、下記日程で中間評価論文公聴会を開催いたします。
ご興味のある方は、ご参加ください。

開催日程：2021年8月24日（火）
開催場所：システム棟２階セミナー室
【必ずマスク着用してください。】

プログラム及び要旨集は以下のとおりです。
【プログラム及び要旨集について、当日、印刷したものは用意いたしませんので、
参加される場合は、各自、必要に応じて印刷したものをご持参のうえ、
ご参加ください。】

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2021年度（９月期）　生命機能研究科中間評価論文公聴会プログラム

（実施会場：生命システム棟２階セミナー室）

セッション	日程	時間	氏名	論文題目	主査	副査１	副査２	座長
1	8月24日	15:45-16:00	ﾚﾝ ｳｶ 練　雨佳	Development of an olfactory receptor signal detection system with the comparable sensitivity to the human olfaction (ヒト嗅覚に匹敵する感度を有する嗅覚受容体シグナル検出法の開発)	黒田　俊一	倉橋　隆		平岡　泰 倉橋　隆
		16:00-16:15	ﾀﾞﾝ ﾗﾝ 段　瀾	Mitochondrial degradation in the oleaginous yeast *Lipomyces starkeyi* (油脂酵母*Lipomyces starkeyi*のミトコンドリア分解)	平岡　泰	野田　健司	岡本　浩二	
		16:15-16:30	審　査　会					

Development of an olfactory receptor signal detection system with the comparable sensitivity to the human olfaction

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Visual and auditory information has been digitized and can now be accurately recorded and played back with video and music, respectively. Olfactory information can be digitized by electrical sensors using semiconductor devices and odorant molecule-specific binding membranes. However, these sensors could not record accurately how the human olfaction perceives the odorant molecules (i.e., human sense of smell), because their recognition properties are very different from those of human olfactory receptors (ORs, 388 subtypes). Therefore, several groups including us have been trying to avoid the issue of odorant molecule recognition of these electrical sensors by expressing all human ORs in cultured cells as odorant sensors. We have developed an odorant sensor with cells expressing 388 human OR subtypes individually and used it to detect the target odorant molecules digitally. The sensitivity of this odorant sensor to odorant molecules, unfortunately, was not as high as in human endogenous ORs. In olfactory neurons, the binding of odorant molecules to OR activates adenylate cyclase via the G protein $G_{\alpha olf}$, which increases intracellular cAMP levels, opens cyclic nucleotide-gated (CNG) channels, and allows the influx of extracellular calcium ions. This intracellular signaling pathway is regulated by a negative feedback mechanism by the incoming calcium ions and causes desensitization of the OR response.

In this study, we have established stable cell line to express OR51E1, trimeric G protein-subunit (containing $G_{\alpha olf}$), CNG, and molecular chaperons. This stable cell line mimics human olfactory sensory neuron having the OR-mediated signaling pathway and the desensitization machinery of the OR response. However, the cell line often shows low sensitivity compared to the sensitivity of olfactory receptors of human olfactory sensory neurons. Therefore, by suppressing the expression of the proteins involved in this desensitization machoinery with siRNAs or various drugs, we successfully increased the sensitivity of OR response. This method is applicable to other ORs and could increase the sensitivity of our odorant sensor effectively.

Mitochondrial degradation in the oleaginous yeast *Lipomyces starkeyi*

(油脂酵母 *Lipomyces starkeyi* のミトコンドリア分解)

Laboratory of Mitochondrial Dynamics (Koji Okamoto Lab.) 32A19077, Duan Lan

Emerging evidence implicates the vital role of mitochondria in lipid consumption and storage, highlighting the intimate link between energy production and saving. The oleaginous yeast *Lipomyces starkeyi* has industrial potential as an excellent alternative lipid producer that is capable of accumulating storage lipid in excess to 65% of its dry weight. Although formation of giant lipid droplets, which is the key hallmark of *L. starkeyi*, appears to be regulated in response to changes in mitochondrial dynamics and metabolism, technical limitations of genetic manipulation have become an obstacle to uncover the mitochondrial behavior in this non-conventional yeast.

In this study, we successfully integrated the mito-DHFR-mCherry (a mitochondrial fluorescent marker) gene into the *L. starkeyi* 18S rDNA locus and observed, for the first time, mitochondria under various growth conditions using fluorescence microscopy. We found that mitochondria are mostly fragmented in *L. starkeyi* cells under fermentable, non-fermentable, and nitrogen-depletion conditions. Notably, a fraction of mitochondria-specific fluorescent signals was localized to the vacuole, a lytic organelle in yeast, indicating degradation of mitochondria in *L. starkeyi* cells. This possible catabolic event was more predominant in cells under nutrient-poor conditions than that in cells under nutrient-rich conditions, concomitantly with increased lipid droplet formation. Furthermore, degradation of mitochondria under nitrogen-depletion conditions was strongly suppressed in the presence of N-ethylmaleimide, an organic compound that inhibits various cellular processes including autophagy. These results raise the possibility that mitochondrial degradation in *L. starkeyi* cells is dependent on mitophagy, an evolutionarily conserved system crucial for mitochondrial quality and quantity control that selectively sequesters mitochondria via autophagy.

Collectively, our studies provide a new tool to investigate mitochondrial dynamics in *L. starkeyi* cells and propose a possible correlation between mitochondrial degradation and lipid storage in this oleaginous yeast.