

due to inhibition of the EPAC function, because the effect cannot be reproduced with other EPAC inhibitors, such as CE3F4, EPAC5376753 and ESI-05. Rather, the effect of ESI-09 and HJC0197 was attributed to their previously unknown action of uncoupling the mitochondrial electron transport chain (ETC). We found that ESI-09 and HJC0197 induced mitochondrial proton leak, causing ATP deficiency and cell death via the following three mechanisms: 1) decreased mitochondrial ATP production due to ETC uncoupling, 2) increased ATP consumption resulting from reversal of F0/F1-ATP synthase/ATPase to maintain the mitochondrial membrane potential, and 3) glucose deficiency as a result of increased glucose consumption due to a compensatory stimulation of glycolytic ATP production. The energy-saving phenotype of cancer cells is thought to serve as an adaptive strategy that allows cell survival in an energy-restricted, acidic tumor microenvironment. Our results suggest that ESI-09 and HJC0197 disrupt bioenergetic tumor metabolism for energy homeostasis in both acidic and neutral microenvironment, and may exert a therapeutic effect against the starvation-resistant phenotype of cancer cells. The complete chemical structures of ESI-09 and HJC0197 will be divulged at the time of the presentation at the meeting.

P2-03

Evaluation of Yanagihara facial nerve grading system based on a muscle fiber analysis of human facial muscles

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【Purpose】 We morphometrically analyzed human facial muscles, and evaluated the Yanagihara facial nerve grading system using our data.

【Methods】 We used 15 types of human facial muscle, two types of masticatory muscle and two types of skeletal muscle. The materials were obtained from 11 Japanese

male cadavers aged 43-86 years. We counted the muscle fibers and measured the transverse area of the muscle fibers (TAMF), and then calculated the number of muscle fibers (NMF) per mm² and the average TAMF.

【Results】 We found a significant correlation between average TAMF and NMF ($r=-0.70$; $p<0.01$). We classified facial muscles into three types based on the correlational results. Type A had a low average TAMF and high NMF. Type C had a high average TAMF and low NMF. Masticatory and skeletal muscles were characterized as Type C. Type B was intermediate between Types A and C.

【Conclusions】 Pathological changes in the facial muscles in facial nerve palsy seem to vary according to the type of facial muscle, because each facial muscle has a unique fiber-type composition. As the nine discrete facial expressive states evaluated in the Yanagihara system involve all three facial muscle types of our classification, the Yanagihara system is an outstanding system for grading facial nerve palsy in terms of the facial muscle morphology.

P2-04

Effect of phosphorylated estrogen receptor alpha on apoptosis in human endometrial epithelial cells

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Estrogen receptor alpha (ER α), together with estradiol plays a critical role through its target molecules in control of cell growth and differentiation. The activities of ER α itself can be modulated by epidermal growth factor (EGF), insulin-like growth factor-I via the phosphatidylinositol 3-kinase (PI3K)/AKT pathway in breast cancer cells. To clarify how ER α functions are regulated in endometrial cells, molecules related to phosphorylation of ER α were examined. It was found that the expression of phosphorylated p-AKT1/2/3 (Thr 473) was increased