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Author(s)	Mung, KL; Wong, NS
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Poster Number

34 **Use of a Tunable Resistive Pulse Sensing System to Detect Drug Response from the Mitochondria at Organelle Level**

Loo Fong Chuen (CUHK)
(Supervisor: Professor Kong Siu Kai, CUHK)

Single organelle analysis from cancer cells provides a better understanding of the drug effects from the isolated organelles for anti-cancer drug development. Since mitochondria play a key role in regulating the life and death of cancer cells, we have developed a nanometer-scale sensing technique using the Tunable Resistive Pulse Sensing (TRPS) system to compare the drug response from single mitochondrion (diameter around 500 nm) isolated from the liver cancer cells with or without multidrug resistance (MDR).

This TRPS technique is based on the detection of blockade events when mitochondria pass through a tunable nano-pore for the change in time duration and current magnitude after drug treatment. In this presentation, the use of the TRPS system for the detection of mitochondrial response upon drug treatment will be highlighted. We first optimized the experimental conditions and verified the system by gold nanoparticles, and then applied the system to detect the drug response from single mitochondrion isolated from cancer cells. We found that more mitochondrial damages include mitochondrial swelling and change in surface charge were observed in the cancer cells with MDR when compared to that without MDR after anti-cancer drug candidate polyphyllin D treatment.

35 **The enzymatic mechanism mediating the breakdown of glycogen in hypoxic tumor cells**

K.L.Mung[1] , N.S.Wong[1]
1.Department of Biochemistry, The University Of Hong Kong

Glycogen has been recently implicated as a major source of metabolic fuel for hypoxic tumor cells. The biochemical mechanism underlying the breakdown of glycogen to produce the substrate for glycolysis though is not fully understood. The aim of this study is to demonstrate the potential role of glycogen phosphorylase or α-glucosidase in mediating breakdown of intracellular glycogen in hypoxic tumor cells. The deprivation of glucose in normoxic tumor cells over a period of 6 hours resulted in marked reduction of intracellular glycogen level. Imposing hypoxia (1% O2) on these cells during the last three hours of glucose deprivation accelerated the decrease of intracellular glycogen content. The co-incubation of cells with a specific glycogen phosphorylase inhibitor (GPI) but not a α-glucosidase inhibitor (miglitol) prevented the loss of intracellular glycogen seen in glucose-deprived cells under normoxic condition. However, GPI or miglitol alone or together had no effect on the enhanced loss of glycogen seen in the hypoxic cells. Results of in vitro enzyme assays for glycogen phosphorylase activity extracted from hypoxic cells showed that both the AMP-independent and the AMP-dependent component of the enzyme activity could be effectively inhibited by GPI. Our data suggest that the degradation of intracellular glycogen in hypoxic tumor cells is unlikely to be mediated by either glycogen phosphorylase or α-glucosidase. Further confirmation of this hypothesis will be achieved by knockdown experiments of glycogen phosphorylase expression decreased after hypoxic treatment.