

## **Seminar**

### **ATP-citrate lyase deficiency highlights critical sources of lipogenic acetyl-CoA and intracellular organelle crosstalk**

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Proliferating cells rely on fatty acid synthesis and acetyl-CoA generation to support membrane biogenesis and acetylation. Within the tumour microenvironment cancer cells must negotiate fluctuating nutrient levels and other stresses, so understanding how cells maintain acetyl-CoA levels for lipogenesis in these contexts is critically important. To this end we applied  $^{13}\text{C}$  isotope tracing to cell lines deficient in these mitochondrial (ATP-citrate lyase; ACLY-), cytosolic, (acetyl-CoA synthetase (ACSS2-) and peroxisomal (peroxisomal biogenesis factor 5; PEX5-) dependent pathways. Metabolic tracing and knockout studies link peroxisomal oxidation of exogenous lipids as a major source of acetyl-CoA for lipogenesis and histone acetylation in ACLY knock out conditions, highlighting a role for inter-organelle crosstalk in supporting cell survival in response to nutrient fluctuations. Further understanding the mechanism of action of FDA approved prodrug, bempedoic acid (BPA) in lowering cholesterol.

***Thursday, Aug 10<sup>th</sup> 2023***

***11:30 AM (Tea / Coffee 11.15 AM)***

***Auditorium, TIFR-H***