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PROGRAM BOOKLET

THURSDAY 30TH - FRIDAY 31ST JULY 2020

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ABSTRACTS
Poster Session

P45. Inhibition of PARG activity affects lysosomal function and hampers *T. cruzi* infection in Vero cells

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Chagas disease is a potentially life-threatening protozoan infection with little therapeutic alternatives. Since *Trypanosoma cruzi* triggers different host cell signaling pathways, targeting them can be therapeutically valuable. Poly(ADP-ribose) (PAR) participates in host cell response during the infection: Poly(ADP-ribose)Polymease-1 inhibition or silencing decreases *T .cruzi* infection and Poly(ADP-ribose)glycohyrolase (PARG) inhibition or silencing almost completely abrogates it. New results showed PAR raised early after infection (15 min) and remained elevated. *T. cruzi* invades the host cell by lysosome-independent, lysosome-dependent or autophagic pathways. However, they must all culminate in the fusion of the trypomastigote-bearing parasitophorous vacuole (TcPV) to lysosomes. PARG inhibition or silencing during the invasion step caused a significant reduction in *T. cruzi* cell invasion. Absence of PARG activity didn´t hamper formation of TcPV with early endosomal characteristics (EEA1+ or PIP3+ vacuoles), nor infection levels under nutritional stress, suggesting PARG is unimportant in early lysosome-independent and autophagic pathways. However, PARG activity seems crucial for lysosomal function: PARG-silenced or inhibited cells reduced DQ-BSA Red and Lysotracker DND-99 staining, indicating proteolytic activity and pH are altered. LAMP-1 signal was also drastically reduced. PARG activity seems important for the maintenance of lysosomal activity, and, therefore, for the initial steps of *T. cruzi* infection.