Track: Modeling Development and disease - Epithelial_gut

MODELING HOST-PARASITE INTERACTION IN CHAGAS DISEASE WITH MURINE INTESTINAL ORGANOIDS

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Chagas disease (CD) is a potentially life-threatening illness caused by the parasite *Trypanosoma cruzi* (*T. cruzi*). With around seven million people infected worldwide and over 10,000 deaths per year, CD is a major public health issue in Latin America. The main route of transmission to humans is through a triatomine bug (vector-borne) and, to a minor extent, by blood transfusion, organ transplantation, laboratory accidents, congenitally and orally (food-borne). The acute phase of CD presents mild symptoms. If left untreated, it develops into a long-lasting chronic illness, characterized by severely impaired cardiac, digestive, and neurological functions. The intestinal tissue appears to have a key role during oral transmission and chronic infection of CD. In these immune-privileged reservoirs, dormant/quiescent parasites have been suggested to contribute to disease persistence, infection relapse, and treatment failure. However, the interaction between the intestinal epithelium and *T. cruzi* has not been examined in depth, in part, due to the lack of *in vitro* models resembling the biological and structural complexity of this organ.

Therefore, to understand the pathophysiological role played by the intestinal tissue during transmission and chronic infection, we evaluated the progression of *T. cruzi* infection of murine colon organoids. In order to model CD, 3D and 2D systems of murine intestinal organoids were infected with *T. cruzi* Dm28c, a strain that has been associated with high virulence and oral outbreaks. At different time points, the presence and load of parasites in the organoids, as well as the host cell morphology were evaluated by confocal microscopy, and compared to those obtained with a classical infection model (Vero cells).

We show that the parasite invades and replicates in intestinal epithelial primary cells grown as intact organoids (3D) and monolayers (2D). The permissiveness to pathogen infection differed markedly between the primary and the tumoral (Vero) cells. So far, this represents the first evidence of the potential of these nearly physiological cellular systems to study host-pathogen interaction for CD and/or for the future evaluation of anti-chagasic drugs.