

***Theileria*-induced host cell transformation: a matter of 'divide and rule'**

Dirk Dobbelaere, Division of Molecular Pathobiology, DCR-VPH, Vetsuisse Faculty, University of Bern.

Theileria parva and *T. annulata* are two intracellular parasites of cattle that are transmitted by ticks and cause severe lymphoproliferative diseases called East Coast Fever and Tropical Theileriosis. East Coast Fever (*T. parva*) is prevalent in Sub-Saharan East and Central Africa, whereas Tropical Theileriosis (*T. annulata*) occurs in the Mediterranean region, the Middle East, and large areas of Asia including the Indian subcontinent.

The parasite differs from several other apicomplexan parasites in that it does not reside in a parasitophorous vacuole. Shortly after entry, the parasite dissolves the surrounding host cell membrane and continues its development free in the host cell cytoplasm. A unique feature of *Theileria* infection is that it causes the uncontrolled proliferation of the cells it infects. This is achieved by dialling into the signal transduction networks that regulate host cell proliferation and survival. One striking example is the direct activation of the transcription factor NF- κ B by the recruitment and activation at the parasite surface of IKK, a pivotal regulatory kinase of the NF- κ B pathway. Together with several other important pathways that are activated indirectly, this results in the constitutive induction of anti-apoptotic mechanisms and stimulating G1 to S cell cycle progression.

By inducing uncontrolled cell proliferation, the parasite also faces the challenge of having to make sure that the schizont is divided over the two daughter cells each time the host cell divides. We established that the schizont usurps the host cell mitotic machinery to ensure its persistence. The schizont first dynamically interacts with newly formed host cell microtubules that emanate from the spindle poles and during anaphase assembles host cell central spindles at its surface. As part of this process, the schizont recruits host cell Plk1 and parasite association with host cell central spindles appears to require Plk1 catalytic activity. By hijacking the central spindle which functions as an important signalling platform that regulates cleavage furrow formation and cytokinesis, the schizont is strategically positioned to be included in the plane of cell division.