CDK–Cyclin-Driven Cell Cycle Regulation in *Theileria annulata*: Molecular Insights and Therapeutic Opportunities

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Theileria annulata is a tick-transmitted apicomplexan parasite spread by *Hyalomma* spp. that infects bovine leukocytes and causes bovine tropical theileriosis (BTT), a disease responsible for annual economic losses exceeding US$1.3 billion in India. Distinct from most protozoan pathogens, *T. annulata* induces a reversible oncogenic transformation of infected B cells, macrophages, and dendritic cells, promoting sustained proliferation and resistance to apoptosis. This cancer-like phenotype highlights parasite encoded signalling pathways, particularly protein kinases, as attractive therapeutic targets. Building on previous kinome profiling that identified 54 protein kinases encoded by *T. annulata*, the present study focuses on the systematic characterization of cyclin-dependent kinases (CDKs) and their regulatory cyclins central orchestrators of cell cycle progression and transcriptional control. In-silico analyses resolved eight TaCDKs and four TaCyclins, and their transcriptional expression was validated by quantitative RT-PCR. Yeast two-hybrid assays demonstrated that individual TaCyclins interact with multiple TaCDKs, suggesting the assembly of flexible and potentially stage-specific regulatory complexes. Stage-resolved immunolocalization using affinity-purified polyclonal antibodies revealed distinct spatial distributions of TaCDKs and TaCyclins in schizont and merozoite stages. Furthermore, colocalization analyses during synchronized S and G2/M phases uncovered dynamic CDK-cyclin associations, implicating these complexes in coordinated regulation of parasite proliferation and host cell transformation. Together, these findings establish the first integrated functional framework of CDK-cyclin networks in *T. annulata*. By defining kinase modules that underpin parasite-driven cellular reprogramming, this study positions CDK-cyclin complexes as high-value molecular targets for selective kinase-based interventions and advances translational strategies to combat tropical theileriosis worldwide, highlighting their relevance for next-generation antiparasitic drug discovery, rational target prioritization, and development of host-directed therapeutic approaches capable of disrupting parasite persistence, limiting disease severity, and improving sustainable livestock health