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as the rise in the intracellular Ca2+levels, causing the disruption of the actin filaments. Finally, an arrest of the cell cycle at the G0/G1 phases produced by these EVs is also confirmed by flow cytometry and Western blot. This work seeks to elucidate the way in which EVs influence certain aspects of the cell physiology that favour the establishment of this parasite inside the host cell.

Poster 59 : Condensin complex contributes to VSG expression, regulation and switching in *Trypanosoma brucei*

Presenter: **Dr Domingo Rojas**, *Post-doctoral researcher, IPB "López-Neyra", CSIC*

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African trypanosomes evade the host immune response by periodically changing their protein coat, constituted by a single Variant Surface Glycoprotein (VSG), allowing for chronic infections. We have previously published that Cohesin complex regulates in situ transcriptional VSG switching, as partial depletion of Cohesin subunits increases the frequency of antigenic variation. Condensin complex, structurally similar to the cohesin complex, has recently emerged in eukaryotes as a mayor regulator of chromosome architecture, chromatin compaction during interphase, and is greatly enriched near highly expressed genes. Previous results suggest that SUMOylation of chromatin at the active VSG locus may function to nucleate factors to the nuclear body ESB, where VSG transcription occurs. Furthermore, we found by proteomic analysis that TbSMC4, a subunit of the condensin complex, is a consistent and abundant SUMO target. Therefore, it seems probable that Condensin functions in the regulation of VSG monoallelic expression and/or transcriptional switching. Co-IP experiments showed that trypanosome condensin includes well-known subunits CND1 and 2 and SMC4, suggesting a conserved multiprotein complex that localizes in the nucleus, as described in other eukaryotes. In addition, we found distinct SUMOylation sites in the condensin subunits of the infective bloodstream forms. Interestingly, partial depletion of condensin subunits resulted in a significant increase of VSG221 switching off events, reaching up to 10% of the population, a switching frequency higher than previously described for cohesin depletion. Isolated switches corresponded to in situ transcriptional activation events of independent telomeric VSG-ESs. All data suggest that condensin complex has a key role in establishing and/or maintaining the transcriptional state of VSG-ES chromatin.

Poster 60 : Hit-to-lead and target identification studies within a novel class of anti-trypanosomal agents.

Presenter: **Dr Rosario Diaz Gonzalaz**, *Postdoctoral researcher, Spanish Research Council*

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Human African trypanosomiasis (HAT), one of 20 neglected tropical diseases (NTDs) designated by the World Health Organization, affects approximately 8,000 people in the remotest parts of Africa; the disease is devastating to those afflicted. HAT is an insect-borne disease caused by the protozoan parasite *Trypanosoma*

brucei, and once the parasite crosses the blood brain barrier it causes disrupted sleep patterns, brain damage and eventual death. Current treatments for this disease are associated with complex treatment regimens and often result in the development of long-term health issues; in addition, reports of resistance are becoming more frequent, and its immune evasion mechanisms makes challenging the development of vaccines. Combined, these factors contribute to a need for new lead compounds to fill the drug discovery pipeline for HAT.
To this end, we employed a lead repurposing strategy, whereby lead compounds against a human target are screened against the disease-causing parasite. We previously reported the results of a whole organism high-throughput screen of 42,444 inhibitors from the GSK kinase-focused screening collection that led to the identification of 797 sub-micromolar inhibitors of *T. brucei* growth. The structure-activity relationships (SAR), biological profiling and target identification studies within one of these clusters with high potency, excellent selectivity and good absorption, distribution, metabolism, and excretion (ADME) properties will be discussed. The antiparasitic effect of compounds in the series was measured against intracellular *T. cruzi* and *Leishmania donovani* and their host mammalian cell lines, generating a wider view of the potential of these compounds for the treatment of other diseases caused by kinetoplastids such as the leishmaniasis and Chagas disease.

Poster 61 : The epidemiological role of indigenous dogs in transmitting animal and human African trypanosomiasis in Zambia: A case study of dogs from Mambwe district, eastern Zambia.

Presenter: **Mr Malimba Lisulo**, *PhD Student, The University of Edinburgh*

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Throughout their long history of domestication, dogs have been sources of parasite exchange between livestock and humans and remain an important source of emerging and re-emerging diseases including trypanosome infections. A cross sectional survey of Canine African Trypanosomiasis (CAT) involving 237 indigenous dogs was conducted in tsetse-infested Mambwe district, eastern Zambia in October 2012. Presence of *Trypanosoma congolense*, T. b. brucei and zoonotic *T. b. rhodesiense* in dog blood was confirmed by microscopy (5.9%; 95% CI: 2.9 – 8.9%) and LAMP (8.4%; 95% CI: 4.9 – 12.0%). Most carriers did not manifest clinical illness, except for 3 dogs with *T. brucei* subspecies infection that developed corneal opacity. These findings suggested that indigenous dogs carrying zoonotic *T. b. rhodesiense* might play a reservoir role in the sporadic human sleeping sickness cases being reported. Current and on-going research: A cohort of 162 dogs from the same area was enrolled in 2018 to understand their interaction with African trypanosomes. The study also measured changes in health and demographic outcomes, as well as risk factors associated with morbidity and mortality. Follow-ups were done at 3 different time-points: June, September and December 2018 representing the cold, hot and rainy season. A total of 41 dogs were lost to follow-up: 31 (died from ill-health, wild-predators and other causes) and 10 (Sold or relocated from study area). Preliminary results show an overall prevalence of 53% trypanosome infection with half involving zoonotic *T. b. rhodesiense*. As earlier observed in 2012, most of the carriers remained asymptomatic throughout the study. Apart from harbouring trypanosomes, several dogs had endo and