## **135 (56)** APPLYING MACHINE LEARNING TO EXPLORE CORRELATES OF PROTECTION FOR A VACCINE AGAINST *TRYPANOZOMA CRUZI*

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Introduction: Chagas disease, caused by the protozoan parasite *Trypanosoma cruzi (T. cruzi)*, is a tropical neglected disease for which a vaccine has yet to be developed. We previously described a vaccine candidate composed of a trans-sialidase fragment (TSf), and a cage-like particle adjuvant (ISPA). Correlates of protection (CoPs) are immunological biomarkers which can be used to predict the efficacy of a vaccine. Machine learning algorithms can be used as an important tool to establish CoPs.
Objective: to apply machine learning to search for potential CoPs in the development of a vaccine against *T. cruzi*.
Methods: BALB/c mice that received a protocol of vaccination with TSf-ISPA were included in the study. IgG antibodies anti-TSf were measured by ELISA. Delayed hypersensitivity reaction (DTH) was measured 48 h post-inoculation of 5 ug TSf in the footpad of TSf-ISPA treated and PBS-control inoculated mice. Vaccinated and control mice were challenged intraperitoneally with 1000-2000 *T. cruzi*. (n=20 per study). Parasitemia were measured at day 15 post-infection (p.i.) and survival was recorded until day 40 p.i. Python'sscikit-learn library was used to construct machine learning classification models.
Results: Logistic regression models were generated to assess the use of optical density (OD 450 nm) as a CoP for the survival of vaccinated mice challenged with 1000 or 2000 *T. cruzi*. In all cases, the results were obtained using k-fold methodology. In order to consider not only the death-live difference but also the time of survival, a criterion was developed. A classification label of "1" was assigned to each mouse that died before day 21 p.i. (coincident with the peak of parasitemia), and a label of "0" was assigned to each mouse which died after day 21 p.i. or even did not die. This approach yielded a substantial predictive capability. For instance, confusion matrix analysis returned average values of sensibility of 80,5%, specificity of 86%, and an area under ROC curve of 0,84 for data from mice infected with 1000-2000 parasites.
Regarding DTH as a CoP, when logistic regression was used to analyze data after the challenge with 1000-2000 *T. cruzi*, confusion matrix returned average values of 83% sensitivity, 90,5% specificity, and a value of 0,87 for the area under the ROC curve.
For parasitemia studies, to develop the models, the following criterion was used: if parasitemia value of each mice/mean PBS parasitemia>1, a classification label of "1" was assigned to that mouse. If parasitemia value of each mouse/mean PBS parasitemia <1, a label of "0" was assigned to that mouse. After the analysis, lower predictive capacity was obtained as compared with the use of antibodies as CoPs.

Discussion: Results suggest that machine learning models could be used to analyze potential CoPs of vaccine candidates against *T. cruzi*. Higher number of experimental animals may allow to increase the robustness of the models.