ARTIFICIAL INTELLIGENCE-ASSISTED IDENTIFICATION OF POTENTIAL CORRELATES OF PROTECTION IN A VACCINE AGAINST *TRYPANOSOMA CRUZI*

Background: Chagas disease, caused by *Trypanosoma cruzi (T. cruzi)*, remains without a licensed vaccine, and correlates of protection (CoPs) have not been reported. We and others have previously described that the regulatory arm of the immune system, including myeloid-derived suppressor cells CD11b+Gr-1+ (MDSCs), can play an important role during both immunization assays and after *T. cruzi* infection. Depletion of MDSCs with 5-fluorouracil (5FU) during immunization improved the protective capacity of our vaccine candidate composed of a trans-sialidase fragment (TSf), and a cage-like particle adjuvant (ISPA).

Objective: To apply machine learning to identify potential CoPs by integrating biomarkers from both regulatory and effector immune responses for our vaccine candidate.

Methods: BALB/c mice were vaccinated with protocols based on TSf-ISPA immunization with or without 5FU administration. Anti-TSf IgG levels, delayed-type hypersensitivity to TSf, and percentage of CD11b+Gr-1+, CD4+, CD8+ cells in peripheral blood were measured. Mice were challenged with 1700 *T. cruzi* parasites, and survival was recorded until day 35 post-infection (total n=46 mice). A decision tree classification model was trained using immunization and survival data, using different variable sets.

Results: Integrating both effector and regulatory response variables in the decision tree model yielded higher predictive accuracy for CoPs compared to models using individual variables. The integrated model achieved a weighted average precision of 88%, sensitivity of 87%, and f1-score of 88%. The macro average also showed a significant improvement over the model using individual variables ($p<0.05$). The area under the ROC curve increased from 0.36 to 0.80.

Discussion: These findings suggest that machine learning can effectively help to identify potential CoPs for *T. cruzi* vaccines, with integrated variables enhancing predictive power. Future studies with larger sample sizes could further validate these models.

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J. Gamba, E. Borgna, E. Prochetto, L. Rossini, L. Veinticinque, C. Farré, A.R. Pérez, I. Marcipar, M. Gerard & C. Cabrera; "Artificial intelligence-assisted identification of potential correlates of protection in a vaccine against Trypanosoma cruzi"
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