ABSTRACT FACE PAGE

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9. **Presenting Author's Career stage: (check one)**
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10. **Website / twitter handle / other public links (optional): _____**
11. **Is this the research presented in this abstract supported by IMAG MSM-related U01 funding?** No
12. **If the Presenting Author is a trainee, who is the trainee's primary research advisor?** Elsje Pienaar

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TRAINEE POSTER AND ORAL PRESENTATION COMPETITONS:

New to the meeting this year, we are holding *both* a trainee poster competition and a trainee oral presentation competition! If the presenting author is a trainee (i.e., a student at any level or a post doctoral trainee), he/she may enter his/her abstract in the trainee poster competition, the trainee oral presentation competition, or both competitions. Trainees may also submit more than one abstract to the meeting and enter more than one abstract in these competitions. Prizes will be given to the presenters of the top-ranked trainee oral presentation and the top-ranked trainee poster (judged during the meeting by the Program Committee).

13. **If the Presenting author is a trainee, would the Presenting Author like to enter his/her abstract in the Trainee Poster Competition*?** Yes

*Note: Trainees who enter the poster competition are expected to stand by their poster during the scheduled poster sessions and present them to the judges.

14. **If the Presenting author is a trainee, would the Presenting Author like to enter his/her abstract in the Trainee Oral Presentation Competition**?** Yes

**Note: The Program Committee will select the top four abstracts from trainees who elect to enter their abstract into the trainee oral presentation competition, these four trainees will be notified by Feb. 17th, and they will deliver their oral presentations (which will be judged) on the second day of the meeting after lunch.

DRIVING FACTORS IN CYTOTOXIC CELL STIMULATION AS TREATMENT FOR HIV: INSIGHT FROM MATHEMATICAL MODELS

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BACKGROUND: Immunomodulatory drugs could be part of a functional cure for human immunodeficiency virus (HIV). One promising immunotherapeutic is the IL-15 superagonist N-803. IL-15 promotes maintenance and activation of cytotoxic immune cells. N-803 expanded cytotoxic T lymphocyte (CTL) and natural killer (NK) cell populations and suppressed simian immunodeficiency virus (SIV) in rhesus macaques. However, N-803 efficacy attenuated with continued treatment, partially recovering only after a long treatment interruption. While biological evidence of drug tolerance, immune regulation, and viral escape could explain these dynamics, the relative contribution of these mechanisms has not been quantified.

METHODS: We present a mathematical model of N-803 treatment of SIV-infected macaques that includes CTL and NK cell populations with N-803-dependent proliferation and activation. Models were calibrated to viral and lymphocyte responses throughout three N-803 treatment phases in chronically SIV-infected rhesus macaques. To assess the contributions of drug tolerance, immune regulation, and viral escape, we compared mathematical models with different combinations of these mechanisms. We compared the ability of each model to reproduce experimental data based on Akaike Information Criterion and important qualitative features of the data.

RESULTS: Two minimal models were capable of reproducing the observed SIV response to N-803. In both models, immune regulation strongly reduced cytotoxic cell activation and enabled viral rebound. Either long-term drug tolerance or viral escape (or some combination of the two) were required to account for changes to viral response across long breaks in N-803 treatment.

CONCLUSIONS: We found that less-frequent N-803 dosing and concurrent immune regulation blockade (e.g. PD-L1 inhibition) were both capable of improving long-term N-803 efficacy. However, N-803 may need to be combined with other immune therapies or ART to countermand viral escape from the CTL response. Our mechanistic model will inform such therapy design and help guide future studies.

REFERENCES:

1. Ellis-Connell et al. *Journal of Virology*. 92(3): e01748-17, 2018.

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