ABSTRACT FACE PAGE

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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? Ashlee N. Ford Versypt**

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.

COMPUTATIONAL MODELING OF THE GUT-BONE AXIS AND IMPLICATIONS OF BUTYRATE TREATMENT ON OSTEOIMMUNOLOGY

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INTRODUCTION: The interplay between gut microbiota and the immune system has a pivotal role in the maintenance of bone health. Recently, short-chain fatty acids (SCFAs) produced by gut microbiota have emerged as a key regulatory participant in shaping the immune system. Butyrate, the most versatile among SCFAs, has been observed to have local and systemic effects including inducing the differentiation of peripheral regulatory T cells (T_{regs}) in the intestine and bone marrow [1]. T_{regs} are the central actor of the negative feedback component of the immune system. The interaction between T_{regs} and cytotoxic CD8+ T cells suppress the inflammatory status and promote the production of Wnt10b to increase bone anabolism [2]. However, the therapeutic benefit of butyrate in bone anabolism remains poorly understood.

METHODS: We develop a multi-compartment physiologically-based pharmacokinetics model to track and quantify effects of butyrate on T_{regs} in the gut, blood, and bone (Fig. 1). Additionally, we connect Wnt10b expression enhanced by T_{regs} to bone remodeling [3].

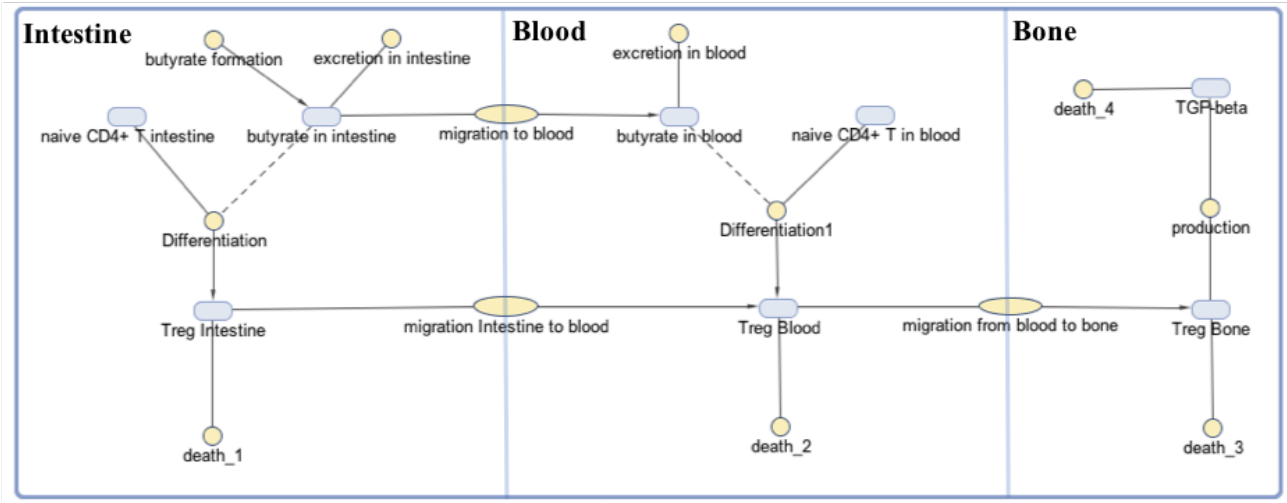

Figure 1: Schematic diagram of butyrate inducing regulatory T cells in the gut-bone axis.

RESULTS: The model shows a sustained release of butyrate in the gut can achieve the experimentally observed biodistribution of T_{regs} in the blood and bone marrow. Additionally, through enhanced Wnt10b expression, changes in osteoblast differentiation and apoptosis rates and rate of bone formation lead to net increases in bone volume.

CONCLUSIONS: The computational approach gives critical insight into the pharmacokinetics of butyrate, biodistribution of T_{regs} in the gut-bone axis, and their contribution to bone formation.

REFERENCES:

1. Furusawa et al. *Nature*. 504(7480):446-450, 2013.
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