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Title: A protease inhibitor from the tick rhipicephalus boophilus microplus attenuated parenchymal destruction in elastase-induced emphysema

Mrs. Clarice 12263 Rosa Olivo claricero@hotmail.com¹, Ms. Juliana 12264 Dias Lourenço juliana.dl31@gmail.com¹, Ms. Francine M. 13005 Almeida faninhbio@gmail.com, Ms. Luana 12265 Paiva Neves luh.neves@gmail.com¹, Ms. Petra 13001 Mello Arantes petramello@gmail.com¹, Prof. Dr Carla 12266 Máximo Prado cmaximoprado@gmail.com², Prof. Dr Iolanda 12267 Tibério iocalvo@uol.com.br MD¹, Prof. Dr Aparecida S. 12270 Tanaka sergio.sasaki@ufabc.edu.br³, Prof. Dr Sérgio D. 12272 Sasaki sergio.sasaki@ufabc.edu.br⁴, Prof. Dr Milton 12274 Arruda Martins mmartins@usp.br MD¹ and Dr. Fernanda 12280 DTQS Lopes fernanda@experimental.fm.usp.br¹. ¹ Medicine, University of Sao Paulo, Sao Paulo, Brazil, 01246000 ; ² Biological Science, Federal University of São Paulo, Diadema, Sao Paulo, Brazil, 09972270 ; ³ Biochemistry, Federal University of Sao Paulo, Sao Paulo, Brazil, 04021001 and ⁴ Center of Natural and Human Science, Federal University of ABC, Santo Andre, Sao Paulo, Brazil, 09210580 .

Body: We showed previously that a protease inhibitor (BMTIA) instillation, 1h after the emphysema induction, attenuated parenchymal destruction. To evaluate if BMTIA could attenuate parenchymal destruction even after the emphysema development. 40 adults C57BL/6 mice were submitted to either a nasal drop of 50 µl of porcine pancreatic elastase (PPE) or saline (S) and 21 days after, animals received 2 doses with 7 days intervals of either BmTIA or vehicle (VE) by nasal instillation. In the end of the BMTIA treatment, animals were anesthetized to evaluate lung function. Airway resistance (RAW), tissue damping (Gtis) and tissue elastance (Htis) were measured using Flexivent small animal ventilator. After sacrifice, lungs were fixed and paraffin embedded for measurements of mean linear intercept (Lm), number of macrophages and MMP-12 positive cells in parenchyma. We observed a significant decrease in Htis values in PPE compared to VE groups. Lm values were increased in PPE groups, whereas the PPE-BmTIA showed a significant decrease in Lm compared to PPE-VE. Compared to VE groups, the number of macrophages and MMP-12 positive cells in parenchyma were increased in PPE groups, whereas the BMTIA treatment reduced MMP-12 positive cells in PPE-BMTIA compared to PPE-VE. There was no significant difference between the groups when we compared Gtis and Raw values. Although treatment with BMTIA has not improved lung function and macrophages infiltration in parenchyma, it reduced the Lm values and the number of MMP-12 positive cells even after the emphysema development, probably due to attenuation in protease-antiprotease imbalance. Supported by FAPESP, LIMHC-FMUSP, Brazil.