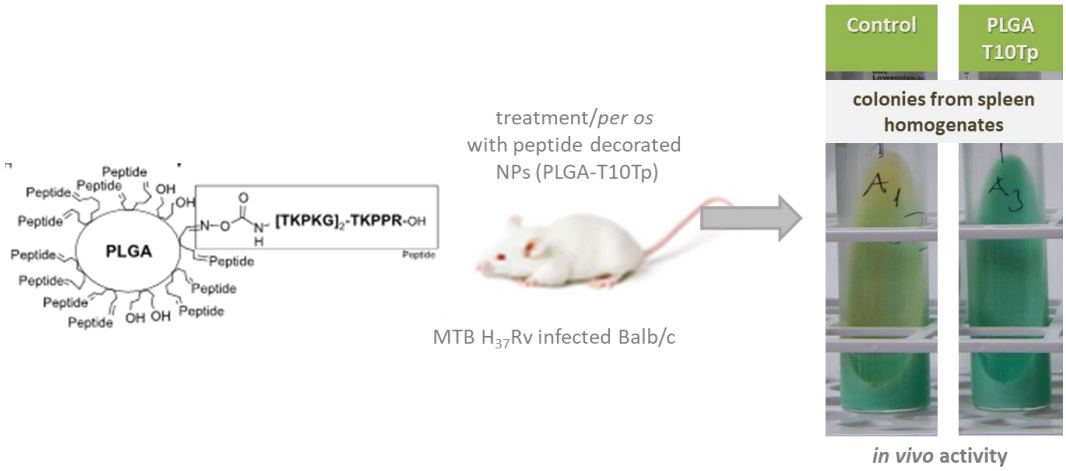
IN VITRO AND *IN VIVO* EVALUATION OF PEPTIDE DECORATED PLGA NANOPARTICLESFOR TARGETED INTRACELLULAR DELIVERY OF ANTITUBERCULOTIC AGENTS: PLURONIC F127 MODIFICATION WITH TUFTSIN

Szilvia Bősze[1], **Kinga Fodor**[2], **Bernadett Pályi**[3], **Gergő Gyulai**[4], **Antal Csámpai**[5], **Gyula Balka**[6], **Éva Kiss**[4], **Kata Horváti**[1]

[1]*MTA-ELTE Research Group of Peptide Chemistry, Eötvös L. University;* [2]*Department of Laboratory Animal Science, University of Veterinary Medicine;* [3]*Hungarian National Biosafety Laboratory, National Public Health Institute;* [4]*Laboratory of Interfaces and Nanostructures, Eötvös L. University;* [5]*Department of Inorganic Chemistry, Eötvös L. University;* [6]*Department of Pathology, University of Veterinary Medicine, Budapest, Hungary*
bosze@elte.hu

In order to enhance the efficacy of antitubercular drug candidates, peptide decorated nanoparticles (NPs) consisting of biodegradable poly(D,L-lactic-co-glycolic acid) (PLGA) carrier were designed. Tuftsin derivative was employed as targeting moiety, that has been reported as a macrophage-targeting peptide[1]. Transformation of the surface modifier, Pluronic F127 hydroxyl groups – which have limited reactivity – into aldehyde groups provides a convenient way to bind aminooxy-peptide derivatives in one step reaction without the need of activating agents. We have also examined that this change has no effect on the physico-chemical properties of the PLGA NPs (size, polydispersity etc.). The peptide funcionalized PLGA NPs showed relevant *in vitro* activity and directly killed intracellular *Mycobacterium tuberculosis* (MTB) $H_{37}Rv$ in infected monocytes[2]. The peptide decorated PLGA NPs were tested *in vivo* on Balb/c mouse MTB infection model. External clinical signs, detectable mycobacterial colonies in the organs and the histopathological findings substantiate the potent chemotherapeutic effect of the *per os* administered drug canditates loaded NPs. Our data demonsrated that coating nanoparticles with Pluronic-tuftsin conjugate markedly increased the internalization rate, intracellular and *in vivo* activity of the encapsulated drug candidates against *Mycobacterium tuberculosis*.
Employing this approach, a large variety of peptide targeted PLGA nanoparticles can be designed for antitubercular drug delivery.



Acknowledgements: This study was supported by Hungarian Scientific Research Fund (OTKA 104275, 115431, 124077), MedInProt Protein Science Research Synergy Program, VEKOP-2.3.2-16-2017-00014, VEKOP-2.3.3-15-2017-00020 and Bolyai János Research Fellowship of the Hungarian Academy of Sciences.

Reference:

1. Horváti K. et al. (**2014**) *Bioconjug Chem*. **25**(12):2260.
2. Horváti K. et. al. (**2018**) *Bioconjug. Chem*. **29**(5):1495.