Anti-inflammatory and anti-bacterial activity of bovine lactoferrin administered by aerosol in airway infections of pre-clinical wt and CF mouse models

Berlutti F
Dip. di Salute Pubblica e Malattie Infettive - Università La Sapienza, Roma (Grant No. FFC#12/2015)
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Background. In the airways, the CFTR genetic defect leads to dysregulation of inflammatory and iron homeostasis that precedes bacterial infection that, in turn, worsens host damage. Lactoferrin (Lf), an iron-chelating glycoprotein of the innate immunity present in airway secretions and secreted by neutrophils in infection/inflammation sites, in addition to the well-known antibacterial activity exerts a key role in inflammatory and iron homeostasis.

Hypothesis and objectives. We suppose that aerosolized bLf can exert a key role on inflammatory and iron dysregulation and reduce infection in pre-clinical CF mouse models of lung infection. Moreover, since Lf is a natural molecule, it shows no side effects and toxicity. In this study we employed bovine milk derived Lf (bLf) as it has been yet used in several clinical trials. Since in CF airways human and bacterial proteases may alter Lf integrity reducing its activity, we hypothesize that nano-delivery of bLf can protect the molecule against proteolysis. The objectives are: 1- to evaluate anti-inflammatory and antibacterial activities of bLf administered by aerosol in mouse models of chronic lung infection; 2- to prepare bLf-loaded nanoparticles (bLf-NANOs) to be aerosolized.

Methods. Bronchial CF cells were used in in vitro experiments; C57BL/6N, CFTR KO and isogenic mice were employed in vivo studies. Bacterial infections were carried out using P. aeruginosa strains.

Results. In mouse models of acute and chronic P. aeruginosa lung infections aerosol administration of bovine Lf (bLf) significantly reduced inflammation, improved the mouse health, and suggested a role in iron homeostasis. Preliminary results in CFTR KO mice seem to confirm the beneficial role of bLf already demonstrated in WT mice and suggest a significant antibacterial activity. The formulation of bLf-NANOs to be aerosolized was optimized and bLf-NANOs were partially characterized. In particular, the stability of bLf-NANOs was shown

Spin-off for research & clinical purposes. This study represents the basis for the development of a preparation for human use to be tested in clinical trial(s).

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References

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