Aerosoltherapy of Monoclonal Antibodies for Respiratory Diseases

R. Respaud1, L. Vecellio1,2, P. Diot1 and N. Heuzé-Vourc’h1

1 Research Centre for Respiratory Diseases INSERM U1100, University F. Rabelais, Tours, 37032, France
2 Aerodrug, Faculty of Medicine, Tours, 37032, France

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Presenting author email: nathalie.vourch@med.univ-tours.fr

Today, biotherapeutic agents, such as monoclonal antibodies (mAbs), constitute the fastest growing sector of the approved pharmaceuticals industry. Their use has greatly changed the management of patients with hematological cancers, autoimmune and inflammatory diseases. With more than 30 molecules already approved and hundreds more in clinical trials, mAbs/antibody-based therapies provide a tremendous opportunity for delivering benefits to patients with both acute and chronic respiratory diseases, which continue to represent a significant unmet medical need. Most therapeutic mAbs are delivered via the blood, but this route is clearly not the most appropriate for large macromolecules that cannot be transported passively across physiological barriers. Aerosoltherapy has been used for the delivery of medicines for > 50 years, mostly small molecules for the treatment of respiratory diseases. Interest in the local administration of mAbs to the lung by inhalation is currently increasing, as a possible means of improving the efficacy and limiting the systemic side effects of these molecules. This non-invasive route is also attractive for the treatment of long-term chronic diseases, because hospitalization is not required, resulting in lower costs to healthcare systems and improved quality of life for patients.

Thus, we evaluated the feasibility and interest to deliver mAbs through the airways, as aerosol, for the treatment of respiratory diseases. Our findings clearly demonstrate that the airways are a relevant route of administration for improving the therapeutic index of mAbs, increasing their concentration within the target organ while limiting their passage into the bloodstream (Hervé et al. (2014); Guilleminault et al. (2014); Respaud et al. submitted).

The success of inhaled antibody treatments depends on the performance of the aerosol generators their ability to deliver effective, reproducible pulmonary deposition, and the stability of the molecules during aerosolization. All these factors must be optimized to achieve the desired pharmacological effect in the lungs. Mesh nebulizers clearly have several technical advantages over jet/ultrasonic nebulizers, MDI and DPI for the delivery of inhaled antibodies. They can deliver large therapeutic doses and limit their degradation during aerosolization (Maillet et al. (2008); Respaud et al. (2014)). In addition, mAb formulations must be adapted to the aerosol device so as to prevent mAb degradation. In particular, mAb concentration and addition of surfactant are critical to maintain their molecular integrity and pharmacological activity during vibrating-mesh nebulization.

Overall, our findings emphasize the relevance and feasibility of using local delivery of mAbs through the pulmonary route, as aerosol to treat lung respiratory diseases (Respaud et al. (2015)).

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Figure 1: Scheme of the development of a drug and device and the proof of concept principle for an antiricin mAb delivered by aerosol.