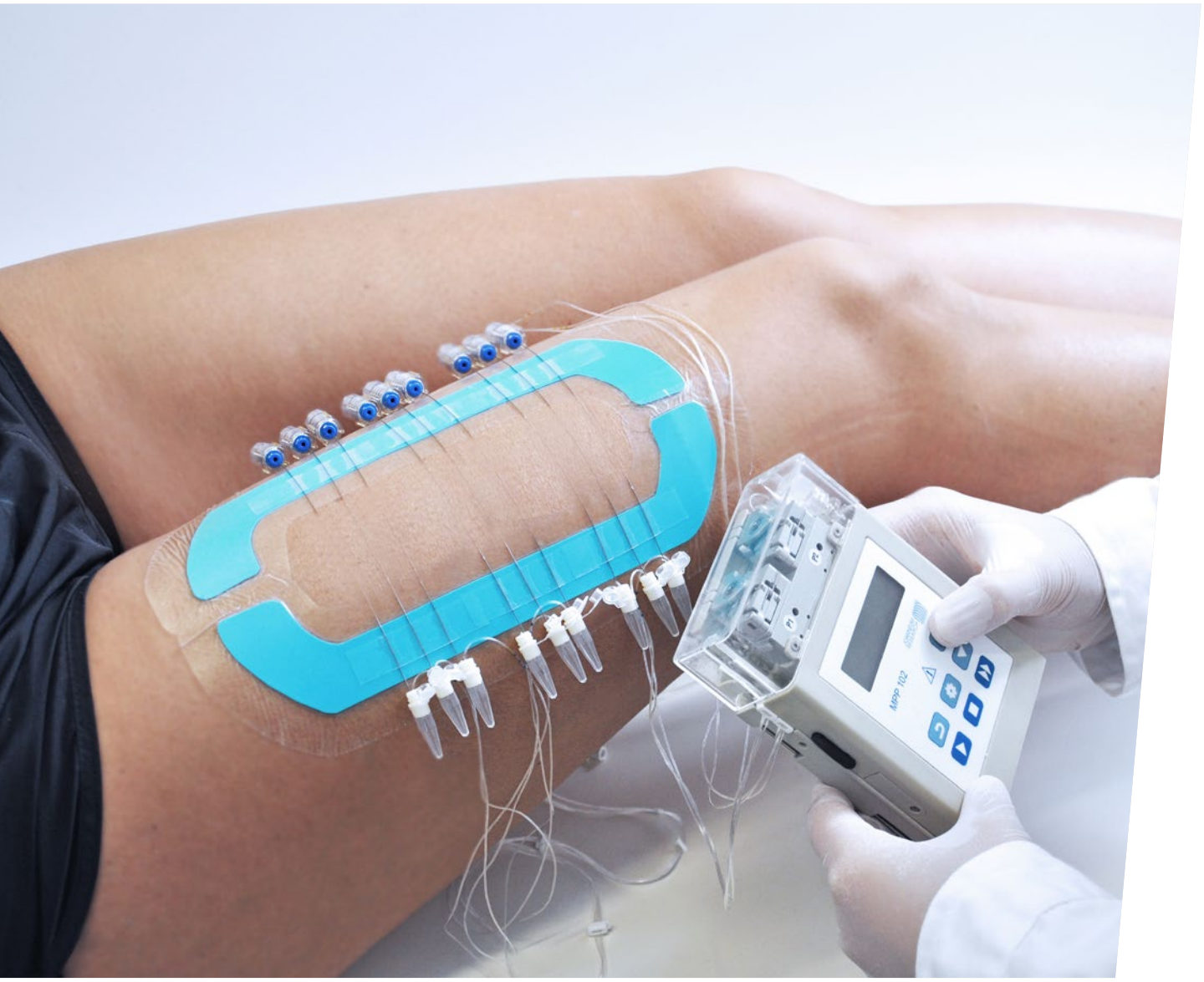
JOANNEUM RESEARCH HEALTH

Project Offer

We are looking for **partners from industry and academia for a collaborative research** project regarding protein binding of drugs.



THE INNOVATION COMPANY

CONTACT: Dr Reingard Raml,
Neue Stiftingtalstrasse 2, Entrance A, Third Floor, 8010 Graz
Phone +43 316 876-42 12 | reingard.raml@joanneum.at
www.joanneum.at/health

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Background:

The degree of protein binding has a huge impact on the pharmacokinetic (PK) and pharmacodynamic (PD) properties of drugs in-vivo. The protein-bound drug fraction serves as a drug depot and delays drug clearance. Only the free drug fraction is pharmacologically active.

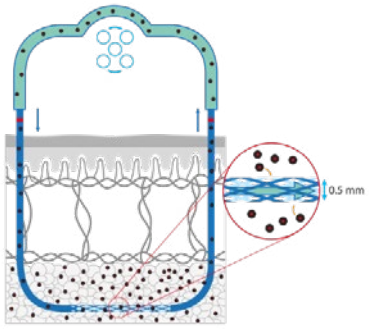
For systemic drugs, protein binding is determined by using routine measurements in blood plasma. For drugs that are designed to act locally in a specific target tissue, protein binding and drug efficiency are influenced by different protein concentration and composition in different tissues. The measurement of **protein binding directly in the target tissue provides thus far more valuable information** than routine blood measurements. Protein binding in different target tissues is poorly understood yet highly relevant for drug development.

Goals:

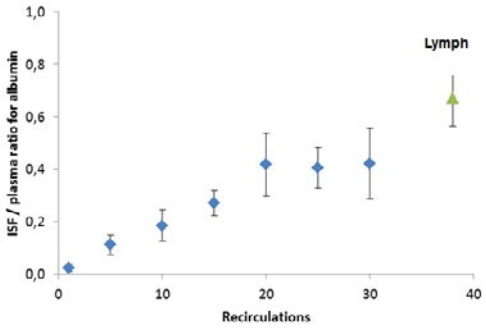
We aim to develop a method to **quantify the free concentration of drugs directly in the tissue**. As a basis for this endeavor, we will quantify the most relevant binding proteins in the tissue and investigate the impact on the binding behavior of drugs. Because in serum it is known that some of these binding proteins are influenced by inflammation we also want to study this impact also directly in the tissue. This may be of high relevance for the PD of drugs that are used in inflammatory diseases.

First Data:

In dermal and subcutaneous porcine skin, we have successfully measured absolute concentrations of albumin, the most relevant binding protein*. We used **recirculation OFM** shown in the left figure below. We identified the most suitable analytical method, **equilibrium dialysis**, to determine protein binding of drugs in low volume and low protein samples.



OFM recirculation setup



Interstital fluid to plasma ratios for albumin after OFM recirculation

Available Technology:

With minimally invasive sampling technologies (open flow microperfusion – OFM or microdialysis – MD) we sample undiluted interstitial fluid. Various bioanalytical methods are available at our lab to determine PK and PD in biological fluids and tissue and methods to assess protein binding. For more information please visit openflowmicroperfusion.com and croservices.joanneum.at

*Hummer, J., Schwingenschuh, S., Raml, R., Boulgaropoulos, B., Schwagerle, G., Augustin, T., Sinner, F., Birngruber, T. OFM-recirculation and OFM-suction: advanced in-vivo open flow microperfusion (OFM) methods for direct and absolute quantification of albumin in interstitial fluid. Biomed. Phys. End. Express. 6, 065031(2020). doi: 10.1088/2057-1976/abc3a7