New Therapeutic Approaches for Peripheral Compression Neuropathies

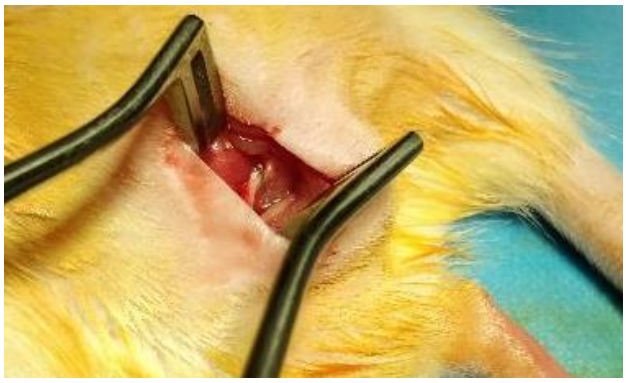

Figure 1: Chronic sciatic nerve compression model with controlled features: Rat sciatic nerve was entrapped using a hemostatic clip that we designed to have a defined lumen size postoperatively (Picture: L. Degrugillier).

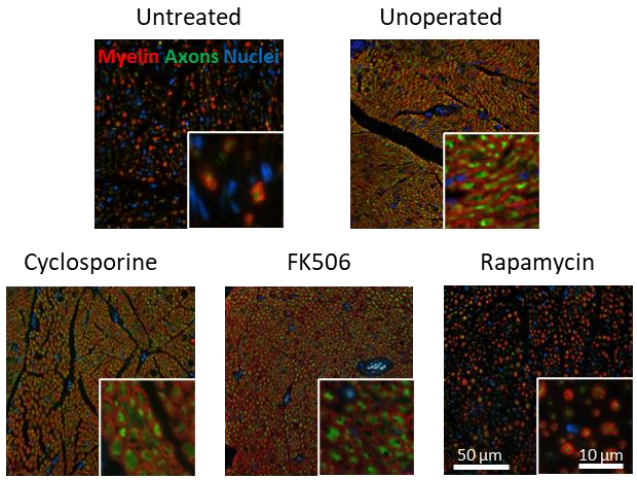

Figure 2: Immuniphilin ligands holds great potential for repair regeneration of chronic nerve compression injury: Systemic drug delivery resulted in functional and anatomical amelioration. This figure shows representative cross sections of the nerves of each treatment group after chronic compression where we can observe that animals treated with Cyclosporine and FK506 show an improved nerve structure preservation (Picture: L. Degrugillier).

PhD-Thesis of Lucas Degrugillier at the Center for Bioengineering and Regenerative Medicine.

Chronic peripheral nerve compressions are a type of neuropathies that can cause paresthesia, pain, numbness and tingling. These neuropathies are caused by the entrapment or the compression of a nerve or its root. Existing treatments are showing limitations and are regularly followed by a surgery to release the injured nerve from compression. Unfortunately, these surgeries are not always successful in curing the symptoms and are also showing some detrimental outcomes. Therefore, the thesis aimed to develop new and effective therapeutic approaches for treating the chronic nerves compression neuropathies.

The first part of the thesis covers the development of new nerve compression model that was achieved by the controlled entrapment of the rat sciatic nerve using a modified hemostatic clip (1). Thus, the chronic injury model with differential injury inputs resulted in different sensory-motor pathophysiological outcome as evidenced by electrophysiological, behavioral and anatomical impairments. Resulting nerve compression model was further employed for drug screening for neuro-muscular protection. Thus, the second part of the thesis covers drug-screening studies in vivo. For this, three FDA approved drugs, cyclosporine, FK506 and rapamycin, were first evaluated *in vitro* for their neurotrophic activity and further *in vivo* as described earlier. Resulting data and knowledge (2), i.e., histological and functional markers appeared to be promising and provides strong basis for further clinical development (3). The third part of the thesis covers the studies on the two novel synthetic molecules inspired from the natural product, paecilomycine A, *in vitro* and *in vivo* (4). The resulting data and knowledge revealed the beneficial effects for neuromuscular regeneration and hold promise for treating the peripheral neuropathies.

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References:

(1) Degrugillier et al. A new model of chronic peripheral nerve compression: for basic research and for drug testing. To be published. 2021

(2) Toll et al. The role of immunophilin ligands in nerve regeneration. Regen Med. 2011

(3) Degrugillier et al. Systematic investigation and comparison of FDA-approved immunosuppressive drugs FK506, Cyclosporine and Rapamycin for neuromuscular protection following chronic nerve compression injury. To be published. 2021

(4) Charkravarty et al. A novel natural product inspired scaffold with robust neurotrophic, neurogenic and neuroprotective action. Sci Rep. 2015