Procaine local effects on skeletal muscles in dysferlin-deficient Bla/J mice.

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Dysferlin is 230kDa transmembrane protein involved in repair of sarcolemma. Mutations in *DYSF* gene lead to dysferlinopathies. Dysferlinopathies are often studied on transgenic mice B6.A-Dysf^{prmd}/GeneJ (Bla/J), that we used to demonstrate regenerative potential of dysferlin after chemical injury by procaine intramuscular injection.

Gastrocnemius muscle of 5 months old Bla/J and C57Bl/6 (control) mice was injected with 100µl of 0,1% procaine (myotoxic agent). Calf muscles were obtained at 2,4,10,14 days after injection and paraffin sections were stained with H&E, immunohistochemically with antibodies against α-SMA (capillary density), myogenin (terminal myogenic differentiation), Ki-67 (proliferation marker), MHC fast/slow (muscular functional activity).

Necrotic muscle fibers (MF) with leukocytes infiltration were found at all time points after injection with gradual reduction (35,1±9,7% vs 8,7±5,4%, respectively, $p<0,001$), in C57Bl/6 this parameter was significantly lower. Percentage of centrinucleated MF in Bla/J was significantly lower at 4 day (11,6±1,18% vs 22,5±4,19% in control, $p=0,03$), remained till 10 days. In Bla/J mice myogenin+ MF maximum was on 4th day after injection (4,4±3,9% vs 9,5±10,01% in C57Bl/6 mice, respectively, $p=0,046$) but significantly lower at all time points comparing with control, which is an indication of activated but incomplete terminal myogenic differentiation. Capillary density was significantly lower in Bla/J mice only on 4th day (0,15±0,04 vs 0,18±0,07 in control, $p=0,03$). Proliferative activity was maximal on 2nd day in both groups (13,77±11,08% in Bla/J vs 19,06±19,7% in C57Bl/6, $p=0,97$) and then decreased till 14th day (0,7±1,09% vs 0,8±1,10%, $p=0,74$). MHC slow/fast staining demonstrated higher ratio of slow MF in Bla/J in compare with control group at all data point with maximum on 10th day (19,6±22,2% vs 0,07±0,4% in control, $p<0,001$).

Conclusion. Procaine injection leads to severe myotoxic lesions of Bla/J mice skeletal muscles and regeneration is slower than in control C57Bl/6 mice. Work supported by Program of Competitive Growth of KFU.