



Shriners Hospitals for Children®
Boston, Massachusetts

LABORATORY OF MOLECULAR PHARMACOLOGY AND PHARMACOLOGICAL IMAGING

Therapeutic drugs of the future will exert their action at precisely defined sites of disease, without affecting any healthy organs. Approaches for engineering such drugs are being developed on the basis of biomolecules and modular molecular constructs.

Our ability to deliver the therapeutic molecules to the sites of disease depends on our understanding of the transport processes and pathways existing in the body that could target the drug to the desired locations. Accordingly, our laboratory at Shriners Hospitals for Children — Boston investigates poorly understood physiological transport processes and pathways, and, when the transport mechanisms are identified, develops new approaches for producing novel therapeutic drugs “riding” on these mechanisms to the desired organs or tissues.

Our work relies on the highly multidisciplinary expertise of our research team and cutting-edge technologies, such as positron emission tomography (PET). Our research has been supported by grants from Shriners, NIH, DoD and the pharmaceutical industry. Our studies resulted in eighteen new technologies, all of which have been transferred to the industry for development and commercialization. Two drugs based on our technologies have recently reached clinical trials. Our collaborative work with the industry has facilitated the preclinical development of seven experimental therapeutics for children, as well as aided the translation of three of them to clinical trials. We also provide methodological support (drug delivery, chemistry, imaging) for other groups working at the Boston Shriners Hospital.

Most recently, our laboratory has become the pioneer in the field of cerebrospinal drug transport (from the cerebrospinal fluid to the brain and meninges). Our data changes the mechanistic understanding of the dynamics of cerebrospinal transport, and opens new opportunities for developing novel therapeutics for several currently untreatable pediatric conditions, such as brain cancer and inherited genetic deficiencies.

Recent Publications

1. Belov VV, Bonab AA, Fischman AJ, Heartlein M, Calias P, and Papisov MI. Iodine-124 as a Label for Pharmacological PET Imaging. *Molecular Pharmaceutics* 2011, v. 8 (3): 736–747.
2. Calias P, Papisov M, Pan J, Savioli N, Belov V, Huang Y, Lotterhand J, Alessandrini M, Liu N, Fischman AJPowell, JL, and Heartlein MW. CNS Penetration of Intrathecal-Lumbar Idursulfase in the Monkey, Dog and Mouse: Implications for Neurological Outcomes of Lysosomal Storage Disorder. *PLoS ONE* 2011 7(1): e30341. doi:10.1371/journal.pone.0030341.
3. Papisov M, Belov V, Fischman A.J., Belova E, Titus J, Gagne M., Gillooly C. Delivery of proteins to CNS as seen and measured by Positron Emission Tomography. *Drug Delivery and Translational Research* 2012, 2:201-209.
4. Papisov M, Belov V, Belova E, Fischman A.J., Fisher R, Wright J, Gannon K, Titus J, Gagne M., Gillooly C. Investigation of intrathecal transport of NPT002, a prospective

therapeutic based on phage M13, in non-human primates. *Drug Delivery and Translational Research* 2012, 2:210-221.

5. Mushti C and Papisov MI. Radioiodination of Aryl-Alkyl Cyclic Sulfates. *Molecules* 2012, 17(11), 13266-13274; doi:10.3390/molecules171113266.
6. Papisov M, Belov VV and Gannon KS. Physiology of the intrathecal bolus: the leptomeningeal route for macromolecule and particle delivery to CNS. *Molecular Pharmaceutics* 2013, 10:1522-1532, DOI: 10.1021/mp300474m.
7. Goldberg A, Khan S, Belov V, Quinn KP, Albadawi H, Broelsch GF, Watkins MT, Georgakoudi I, Papisov M, Mihm MC Jr, Austen W, Yarmush ML. Skin rejuvenation with non-invasive electric fields. *Nature Scientific Reports* 2015, 5:10187, DOI: 10.1038/srep10187.
8. Rotstein BH, Liang SH, Belov VV, Livni E, Levine DB, Bonab AA, Papisov MI, Perlis RH, Vasdev N. Practical radiosynthesis and preclinical neuroimaging of [¹¹C]isradipine, a calcium channel antagonist. *Molecules* 2015, 20; doi:10.3390/molecules200x0000x (In press)

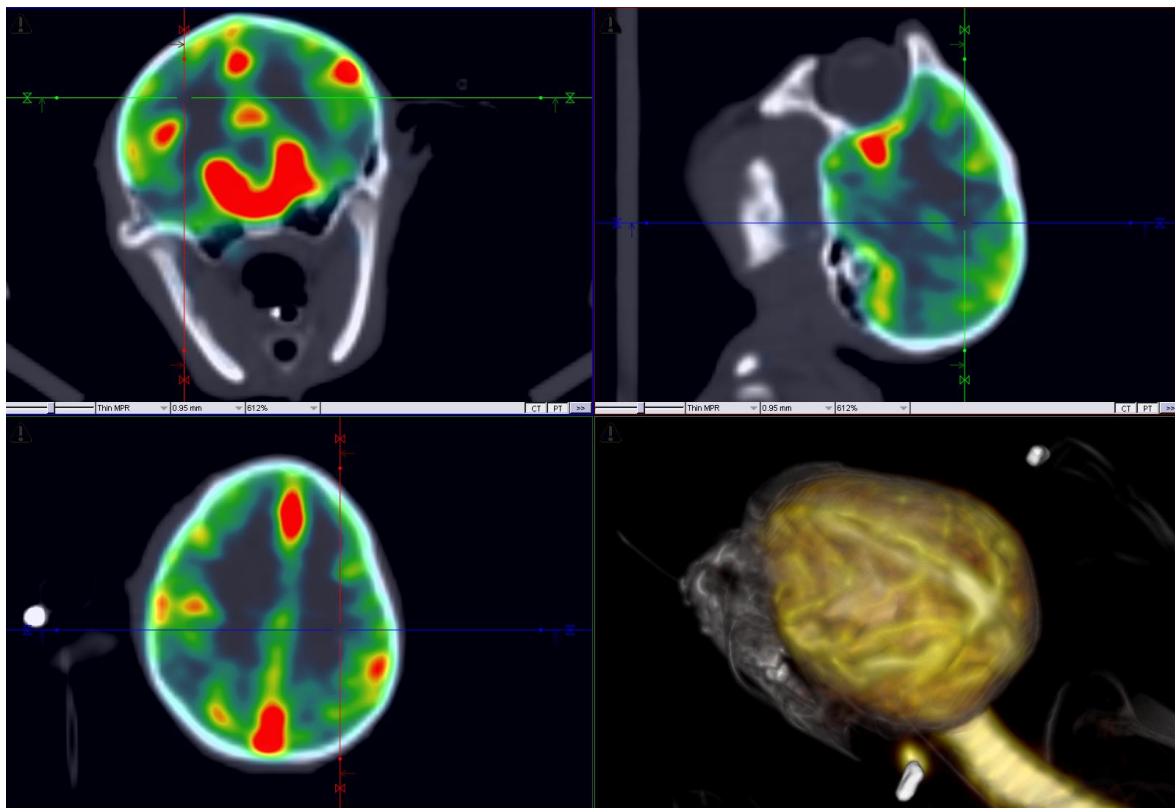


Image provided by Misha Papisov, Ph.D.



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