

Bryan Mackenzie, PhD

Assistant Professor

Department of Molecular and Cell Physiology

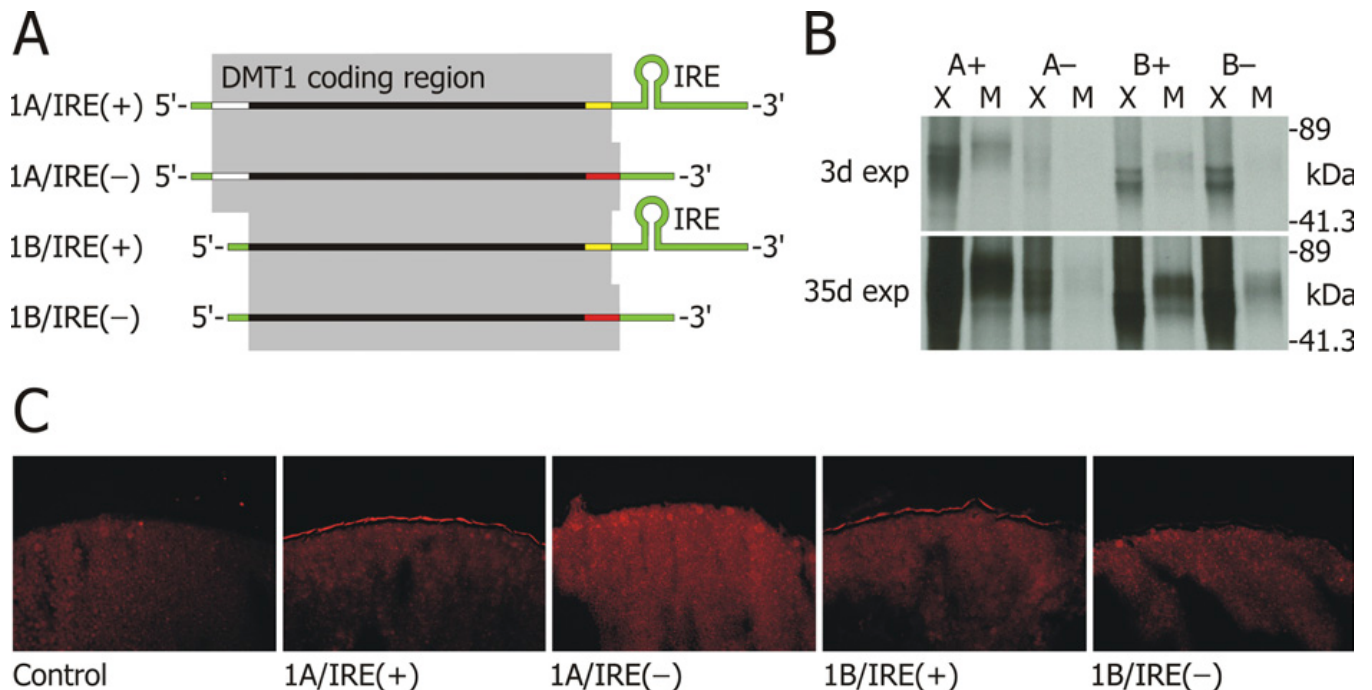
Description of Research:

Iron deficiency is the most prevalent micronutrient deficiency worldwide. Meanwhile iron overload associated with conditions like hereditary hemochromatosis, thalassemia, or sickle cell disease poses a serious threat to many other individuals. The iron transporter DMT1 is the primary route of uptake in the intestine. DMT1 is also responsible for mobilization of iron from the endosome to cytosol, a crucial step in the transferrin-associated uptake of iron in erythroid precursor cells. Dr. Mackenzie's interests lie in the molecular mechanisms, substrate selectivity and structure-function of DMT1. Exploring these aspects of DMT1 will aid in a better understanding of how DMT1 functions in diverse environments and how DMT1 contributes to the etiology of iron overload disorders, such as hereditary hemochromatosis. Structure-function studies may aid in the design of pharmaceuticals, for example, to treat iron overload or heavy-metal toxicity. Additionally, Dr. Mackenzie is studying Na^+ -coupled ascorbic acid (vitamin C) transporter SVCT1 and the System A family of Na^+ -coupled neutral amino acid transporters.

Collaborations:

Dr. Mackenzie collaborates with Dr. Chip Montrose utilizing the live microscopy core to measure metal-ion transport.

Representative Figure:



Multiple isoforms of hDMT1. A. Variant transcripts of the human SLC11A2 gene. There are at least four DMT1 mRNA transcripts (illustrated) that differ in their UTRs (green) and in their coding regions. The 1A exon contains a start codon upstream of that in 1B, adding a 5'-coding region (white) that introduces 29 additional amino acids at the N-terminus of the protein in 1A isoforms. DMT1 transcripts also vary at the 3'-end: those variants containing an IRE in the 3'-UTR, i.e. IRE(+) isoforms, also have an isoform-specific 3' coding region (yellow) in place of the 3' coding region (red) in the isoforms lacking the IRE, i.e. IRE(-). The C-terminus of the IRE(+) forms contains 18 amino acid residues that substitute for the final 25 of the IRE(-) forms. B. Coupled transcription-translation of the multiple isoforms of hDMT1 in a cell-free system, in the absence (X) or presence (M) of canine pancreatic microsomes. L-[³⁵S]methionine-labelled products were separated by SDS/PAGE and the autoradiograph exposed for 3 days (3d exp, upper panel) or 35 days (35d exp, lower panel). A+, 1A/IRE(+)-hDMT1 isoform; A-, 1A/IRE(-); B+, 1B/IRE(+); B-, 1B/IRE(-). Molecular mass of translation products was estimated using Bio-Rad standards of 31.8, 41.3, 89, 131 and 210 kDa. C. DMT1 immunofluorescence in control oocytes and oocytes expressing DMT1 isoforms. Figure 1 from *Biochem J*, 2007; 403:59-69.