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A Novel Enzyme with Spermine Oxidase Activity in Bovine Liver Mitochondria

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The natural polyamines spermine, spermidine and putrescine are polycationic molecules that are involved in various cellular processes, such as cellular proliferation, differentiation, protein synthesis, and signal transduction. They are oxidatively deaminated by amine oxidases and two of their reaction products, H_2O_2 and aminoaldehydes, are involved in many physiophatological processes, including carcinogenesis (1-2).

Recently, a novel enzyme belonging to FAD-containing Polyamine Oxidases (PAO), has been characterized for its capability to oxidase preferentially spermine over acetylated polyamines and spermidine and for this reason designated as spermine oxidase (SMO) (3-4).

SMO was found expressed in nucleus and cytoplasm, while PAOs have been shown to be located mainly in peroxisomes and in cytoplasm (1-2).

As regards the presence of polyamine oxidases in mitochondria, a semicarbazide-sensitive diamine oxidase was recently found in rat liver mitochondrial matrix (MMAO) (5).

To our knowledge, no data about the presence of enzymes with polyamine oxidase activity in other mammalian liver mitochondria are available so far, even if it is well known that polyamines are present and transported into mitochondria (6).

The aim of this study was to investigate the possible presence of enzyme(s) with polyamine oxidase activity in bovine liver mitochondria. Various amines, characterized by different charge distribution and different amine oxidases inhibitors, were used to perform a preliminary kinetic characterization.

Our kinetic results demonstrate that, in bovine liver mitochondria, there is an enzyme with polyamine oxidase activity and that it is inhibited mainly by MDL 72527 over pargyline and semicarbazide. The preferred substrate of this mitochondrial enzyme is spermine; poor activity was found towards acetylated polyamines.

On this basis, we can conclude that, this mitochondrial enzyme, should be a spermine oxidase (SMO). Work is in progress to purify and to localize, in mitochondria, this enzyme to study its physiological role.

References:

1. M. Cervelli, R. Amendola, F. Polticelli F and P. Mariottini (2012). Spermine oxidase: ten years after. Amin Acids, 42: 441-450.

2. RA Jr Casero and AE.Pegg. (2009) Polyamine catabolism and disease. Biochem. J., 421:323-338.

3. Y. Wang, W. Devereux, P.M. Woster, T.M. Stewart, A. Hacker,and R.A. Jr Casero. (2001) Cloning and characterization of a human polyamine oxidase that is inducible by polyamine analogue exposure. Cancer Research, 61:5370-5373.

4. S. Vujcic, P. Diegelman, C.J. Bacchi, D.L. Kramer and C.W. Porter.(2002) Identification and characterization of a novel flavin-containing spermine oxidase of mammalian cell origin. Biochem. J., 367:66. 675.

5. R. Stevanato, S. Cardillo, M. Braga, A.De Iuliis, V. Battaglia, A. Toninello, E. Agostinelli, F. Vianello. (201. Novel copper amine oxidase activity from rat liver mitochondria matrix. Amino Acids, 40:713-720.

6. V.Battaglia, E.Tibaldi, S.Grancara, F. Zonta, A.M. Brunati, P. Martinis, M. Bragadin, M.A. Grillo, G. Tempera, E. Agostinelli, A. Toninello.(2012) Effect of peroxides on spermine transport in rat brain and liver mitochondria. Amino Acids, 42:741-749.