Enzymatic Characterization of *Leishmania major* Phosphatidylethanolamine Methyltransferases *LmjPEM1* and *LmjPEM2*

**Stergios Bibis**

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**Abstract**

Phosphatidylcholine (PC) is the most abundant phospholipid in the membranes of the human parasite *Leishmania*. It is synthesized via two metabolic routes, the de novo pathway that starts with the uptake of choline, and the threefold methylation of phosphatidylethanolamine.

**Objectives**

1. Establish that *Leishmania major* utilizes the methylation pathway involved in PC biosynthesis.
2. Identify putative *Leishmania major* genes involved in the PE methylation pathway.
3. Verify that these putative PE methyltransferase genes are expressed in *L. major* and determine their ability to complement auxotrophy in *Saccharomyces cerevisiae* lacking PE methyltransferase activity.
4. Determine substrate specificities of these enzymes

**Results**

Fig. 7. *LmjPEM1* and *LmjPEM2* complement the choline auxotrophy phenotype of *S. cerevisiae* double null mutant *scpm1(scpm2)* that lacks PEMT activity

Fig. 8. *LmjPEM1* and *LmjPEM2* act as PEMT enzymes

**Conclusion**

- *Leishmania major* posses two PE-methyltransferase genes, *LmjPEM1* and *LmjPEM2*
- *Leishmania major* express both *LmjPEM1* and *LmjPEM2* in both promastigotes and amastigotes in a cell cycle dependent manner
- Which correlates to PE-methyltransferase activity
- Expression of *LmjPEM1* and *LmjPEM2* is independent of choline
- As is PE-methyltransferase activity
- *LmjPEM1* and *LmjPEM2* complement the choline auxotrophy of *scpem1(scpcm2)* yeast deficient of PE-methyltransferase activity
- *LmjPEM1* catalyzes the first and second methylations of PE producing MM-PE and DM-PE
- Albeit with lower affinity for the second methylation
- *LmjPEM2* catalyzes all three methylations of PE producing MM-PE, DM-PE, and PC
- Albeit with a lower affinity for the first methylation

**References**


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