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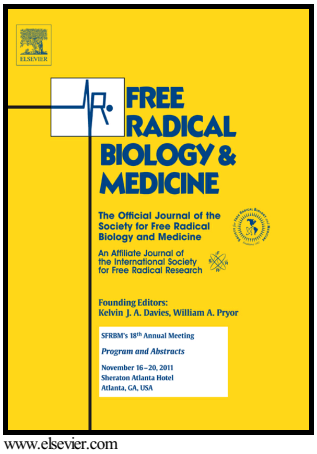

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PII: S0891-5849(17)30753-0
DOI: http://dx.doi.org/10.1016/j.freeradbiomed.2017.09.009
Reference: FRB13447

To appear in: *Free Radical Biology and Medicine*

Received date: 3 July 2017
Revised date: 30 August 2017
Accepted date: 9 September 2017

Cite this article as: K. Veltman, Y. Ahmad, C. Harris and O. Jolliet, Characterizing thiol redox dynamics in the organogenesis stage rat embryo, *Free Radical Biology and Medicine,* http://dx.doi.org/10.1016/j.freeradbiomed.2017.09.009

Characterizing thiol redox dynamics in the organogenesis stage rat embryo

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Abstract

Precise control of the glutathione (GSH):glutathione disulfide (GSSG) balance is vital for the developing embryo, but it is not yet well understood how GSH levels and the GSH redox state are regulated, maintained, and modulated over the course of mammalian embryonic development. In this study, we characterize and connect thiol redox dynamics, protein synthesis, volumetric growth and net cysteine fluxes over the course of early organogenesis (gestational day (GD) 10 to GD11.13) in the rat embryo. Our results show that despite a significant exponential growth of conceptal volumes and protein mass, the GSH:GSSG redox balance is remarkably stable during early organogenesis, with distinct redox potentials for the visceral yolk sac (VYS) (-218mV) and the embryo proper (EMB) (-222mV). The yolk sac was found to play a key role in maintaining GSH levels and the GSH:GSSG redox balance in the developing embryo. Based on an overall cysteine (Cys) mass-balance, we show that until GD10.6, yolk sac supply of Cys, the rate-limiting precursor for GSH synthesis, is sufficient to sustain embryonic demands for its GSH synthesis and protein synthesis needs. After GD10.6, the EMB maintains the amino acid intake flux, resulting in a significant depletion of most thiols in the amniotic fluid and the yolk sac fluid. Cysteine, was found to be predominantly used for *de novo* protein synthesis in the developing embryo (approximately 90% of total Cys). Protein synthesis (rates) should thus be included in any quantitative assessment of GSH redox dynamics in the developing embryo. Our time-course dataset of thiol dynamics, developed exponential relationships for protein synthesis and volumetric growth, and yolk sac surface area-mediated protein influx, provide important quantitative insights in GSH redox dynamics