

## 2. Organ Glutathione Levels after RiboCeine

Roberts, J.C.; Francetic, D.J. [Time course for the elevation of glutathione in numerous organs of L1210-bearing CDF1 mice given the L-cysteine prodrug, RibCys](#). *Toxicology Letters*, 1991, 59, 245-251.

### Study Background

It is well accepted by the scientific community that glutathione levels in cells are homeostatically controlled, and dramatic elevations in glutathione levels are not expected because its biosynthesis is stringently controlled by feedback inhibition<sup>1</sup>. Therefore, glutathione may only achieve a certain level before the biosynthetic machinery would be turned off, regardless of the level of amino acid precursors available in the cell<sup>1</sup>. However, in the presence of a toxic substance that requires glutathione for detoxification, the levels of glutathione in the liver are continually decreasing and virtually depleted in some cases (acetaminophen overdoses). The value of these glutathione elevation studies is not in the “absolute increase of glutathione achieved”, but rather the compound’s ability to maintain glutathione levels under oxidative stress conditions.

Glutathione levels in many organs fall as the result of fasting, and therefore, compounds can be tested in fasting animals for their ability to elevate and maintain organ glutathione.

**Summary:** In this study, RibCys (RiboCeine) was evaluated in fasting mice for its ability to improve glutathione levels in numerous organs at different time points after RiboCeine administration. After 8 to 10 hours of fasting, glutathione levels dropped approximately 43% in the liver, 41% in the bladder, 31% in the kidney, 25% in the heart and 60% in muscle. Other organs, such as the spleen, pancreas, and lung, showed no significant differences in glutathione levels between the two nutritional states.

**Results:** “Glutathione in the liver was elevated 1.5 fold compared to untreated controls at the 16 hour time point. Kidney glutathione also was maximal at 16 hours and achieved 1.6 times control values. Glutathione in muscle achieved 2.5 times the levels in control animals, while the bladder was elevated 2.1 fold and the heart 1.8 fold.”

**Conclusion:** The authors concluded that “RibCys was able to maintain, and, in some organs, continued to elevate glutathione even though the animals were subject to continued fasting”. “The results from the present studies support the hypothesis that RibCys can serve as a reservoir for the crucial glutathione precursor, L-cysteine, and continually supply the amino acid as glutathione synthesis proceeds.”<sup>1</sup> Meister A, J., Glutathione metabolism and its selective modification. *Biol. Chem.*, 1988, 273, 17205-17208.