Communication Regarding Metabonomic Identification of Two Distinct Phenotypes in Sprague-Dawley (Crl:CD(SD)) Rats

Lora C. Robosky,*† Dale F. Wells,* Laura A. Egnash,* Matthew L. Manning,† Michael D. Reily,* and Donald G. Robertson*

*Pfizer Global Research and Development, Metabonomics Evaluation Group, Ann Arbor, Michigan 48105; †Manpower, Inc., Ann Arbor, Michigan 48103

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In a recent publication, we reported the identification and characterization of two distinct phenotypes in Sprague-Dawley rats obtained from the Charles River Raleigh facility (Robosky et al., 2005). The phenotypes were designated as HIP (high hippuric acid level in urine) and CA (high chlorogenic acid metabolites level in urine). The endogenous urinary metabolic profile of each phenotype was distinct and stable over the period from February 2004 through February 2005. The phenotypic difference is most likely due to altered gut flora that play a role in the metabolism of aromatic acids.

Since this time, the phenotype was monitored in Sprague-Dawley rats from Charles River Raleigh facility Room 9 and Room 10 by analyzing urine samples using the same methods. The September 2005 data indicate a shift in the urinary endogenous metabolic profile of urine from Room 9 rats, previously having the CA phenotype (Fig. 1). The urinary levels of hippuric acid and chlorogenic acid metabolites are now similar in Room 9 and Room 10 rats, and the metabolite levels are characteristic of the HIP phenotype.

The observed shift in the CA phenotype was not totally unexpected. A lack of “normal” gut flora speciation was suggested as a possible explanation of the variant CA phenotype observed in rats from Room 9 in the manuscript. It therefore seems possible that during the period from February 2005 to September 2005 a more typical gut flora was established in the Room 9 colony. Of the colonies investigated in the original manuscript, the Room 9 colony represented the most recently initiated colony (December 2002). If this hypothesis is correct, what is surprising is the length of time required for the repopulation of normal gut flora within Room 9 (several years) and the rapidity with which the phenotype changed from the aberrant phenotype (CA) to the more typical HIP phenotype (several months).

These findings in no way invalidate the findings of the original manuscript and highlight a variable not often considered in toxicology studies or any other type of study for that matter. The gut flora are difficult, if not impossible, to completely characterize. However, metabonomics evaluation presents a new opportunity to indirectly measure gut flora composition and its contribution to systems biology. While the impact of gut flora on toxicology as well as other biological investigations has been recognized in principle for quite some time, we believe that this subject is entering an era of renewed interest and importance.

REFERENCES