S9 Performance in the Ames II and Ames MPF™: Aroclor 1254 and Phenobarbital/Naphthoflavone

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Introduction

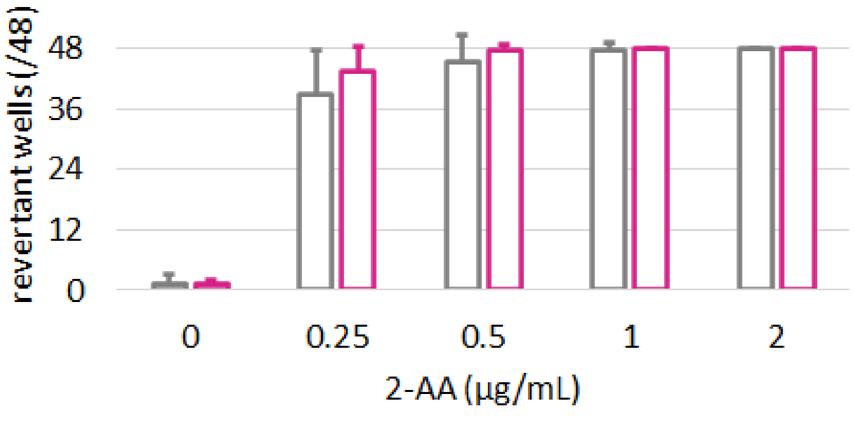
Some chemicals (*e.g.*, aromatic amines or polycyclic aromatic hydrocarbons) are biologically inactive but become mutagenic upon metabolization, often mediated by the cytochrome-based P450 metabolic oxidation system. This system is present in humans and lower animals (mainly in the liver) but absent in bacteria. An exogenous mammalian organ activation system must therefore be included to the Ames test and, for the most part, the metabolic system is taken from rodents.[1]
S9 is manufactured from rat or hamster livers which have been treated with substances causing a strong induction of many xenobiotic metabolizing enzymes. Historically, such substance has often been **Aroclor 1254**, but **β-naphthoflavone and phenobarbital** has also been used.[2,3] A homogenate of the liver is subsequently centrifuged at 9000 g. The resulting supernatant, generally referred to as **S9**, contains microsomes and cytosol, and therefore all microsomal and cytosolic xenobiotic metabolizing enzymes.[3] Other cofactors, including glucose-6-phosphate (G-6-P) and β-nicotinamide adenine dinucleotide phosphate (NADP, for the NADPH-supported oxidation), are added to the system.[1]
As other commercial polychlorinated biphenyls mixtures, Aroclors have been banned in 1977: these mixtures proved to be toxic to humans (with high bioaccumulation in adipose tissue) and have long environmental persistence.[4] As a result, the lots of Aroclor-induced S9 rat liver homogenate were destined to be depleted.
Xenometrix AG, in an effort to provide the best products to the Ames II and Ames MPF™ users, has generated a database of results over the last decade to compare the performance of the Aroclor 1245-induced S9 and the β-naphthoflavone/phenobarbital-induced S9 with well known and studied mutagens requiring metabolic activation, **2-aminoanthracene** (2-AA), **2-aminofluorene** (2-AF) and **benzo[*a*]pyrene** (B[a]P).

Performance of the Aroclor 1254- and PB/NF-induced S9 in the Ames II and Ames MPF™: Historical Data

The average and standard deviation values for dose responses for Aroclor 1254- and PB/NF-induced S9 are shown in grey and pink, respectively.

Aroclor-induced S9 — **PB/NF-induced S9**

TA98



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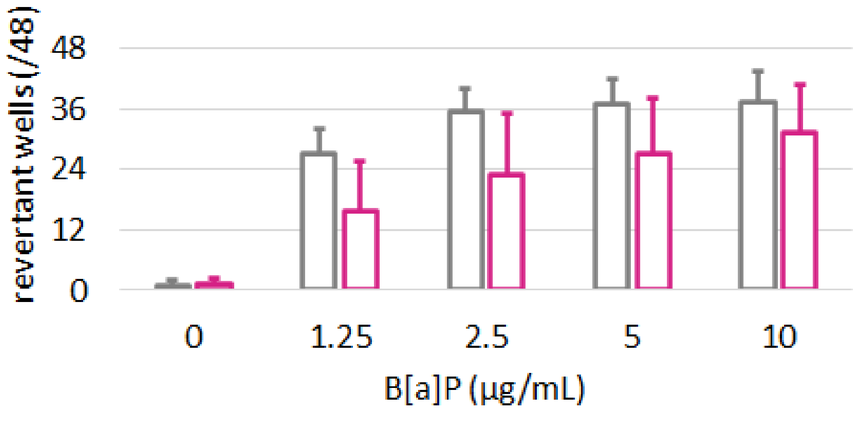

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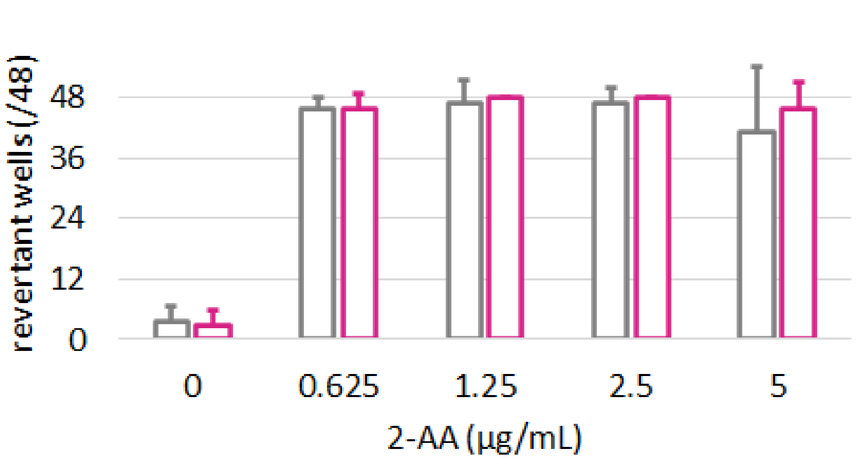
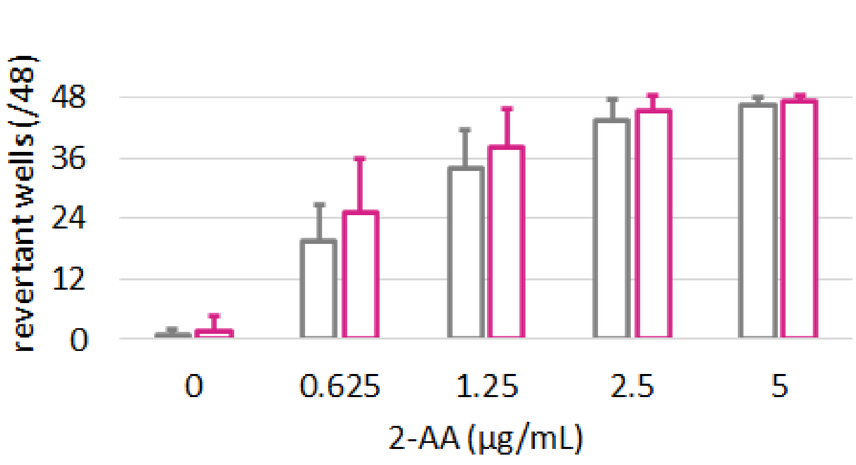


TAMix



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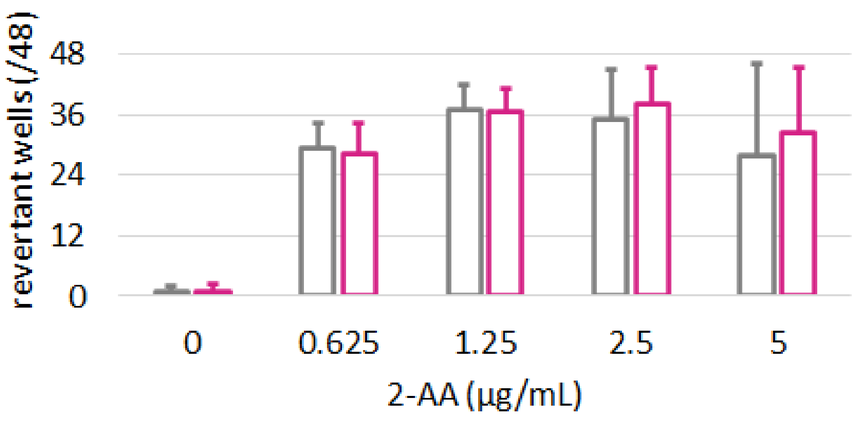

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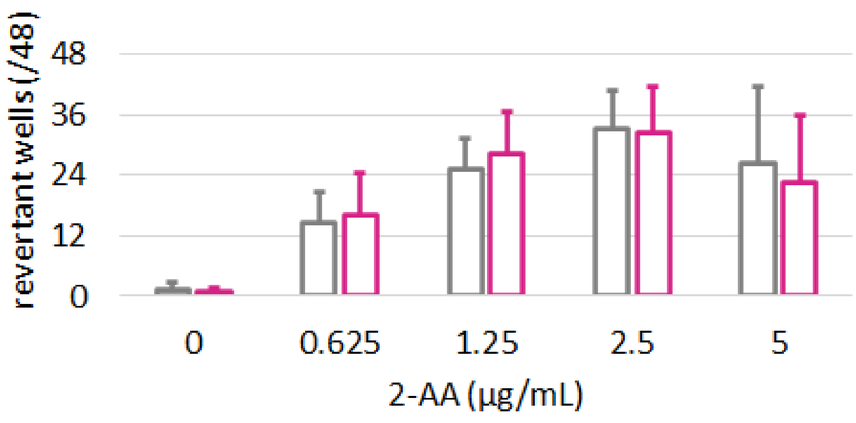
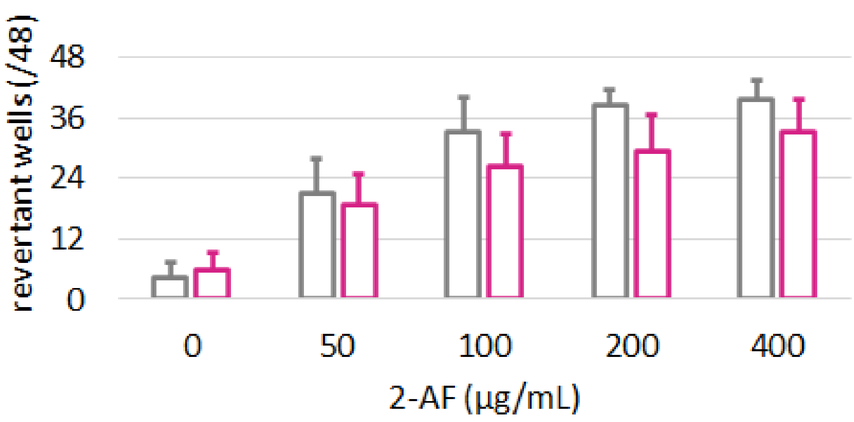
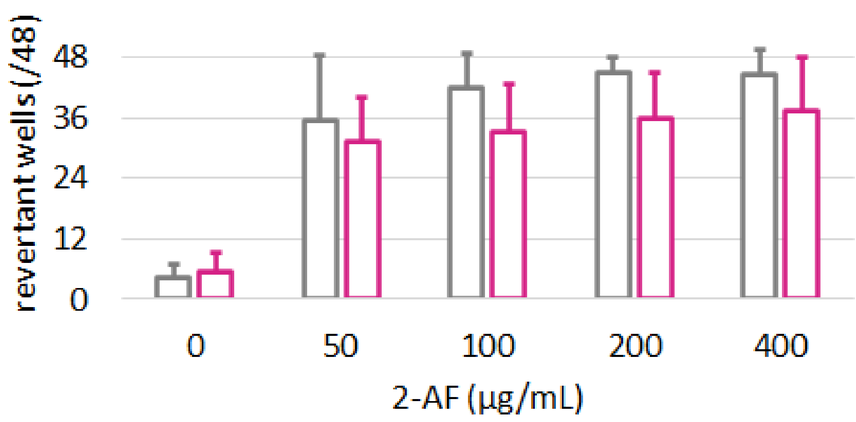


EC Combo



***E. coli* WP2 *uvrA*[pKM101]**



Conclusions

These results suggest that data generated with Aroclor 1254- and PB/NF-induced S9 are essentially identical.

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