

芳香族アミンQSAR共同研究報告

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Genes and Environment

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Local QSAR based on quantum chemistry calculations for the stability of nitrenium ions to reduce false positive outcomes from standard QSAR systems for the mutagenicity of primary aromatic amines



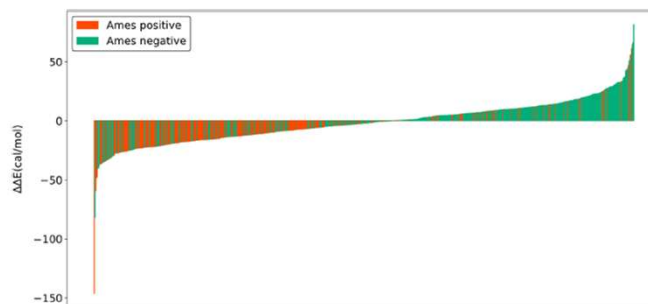
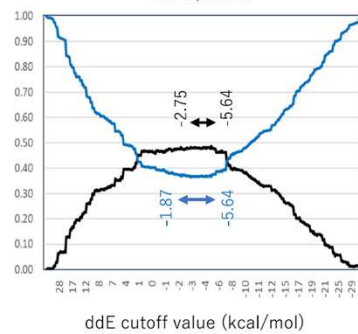
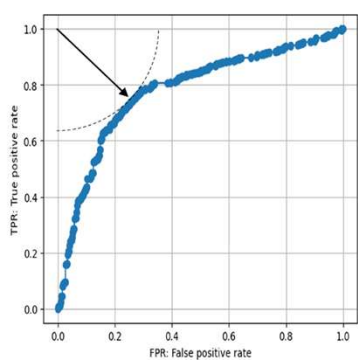
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Table 1 Dataset of primary aromatic amines in this study

Information source	Ames test result		Total
	Positive	Negative	
Total dataset ^a	465	712	1177
Public database	249	171	420
In-house	216	541	757
Working dataset ^b	322	510	832

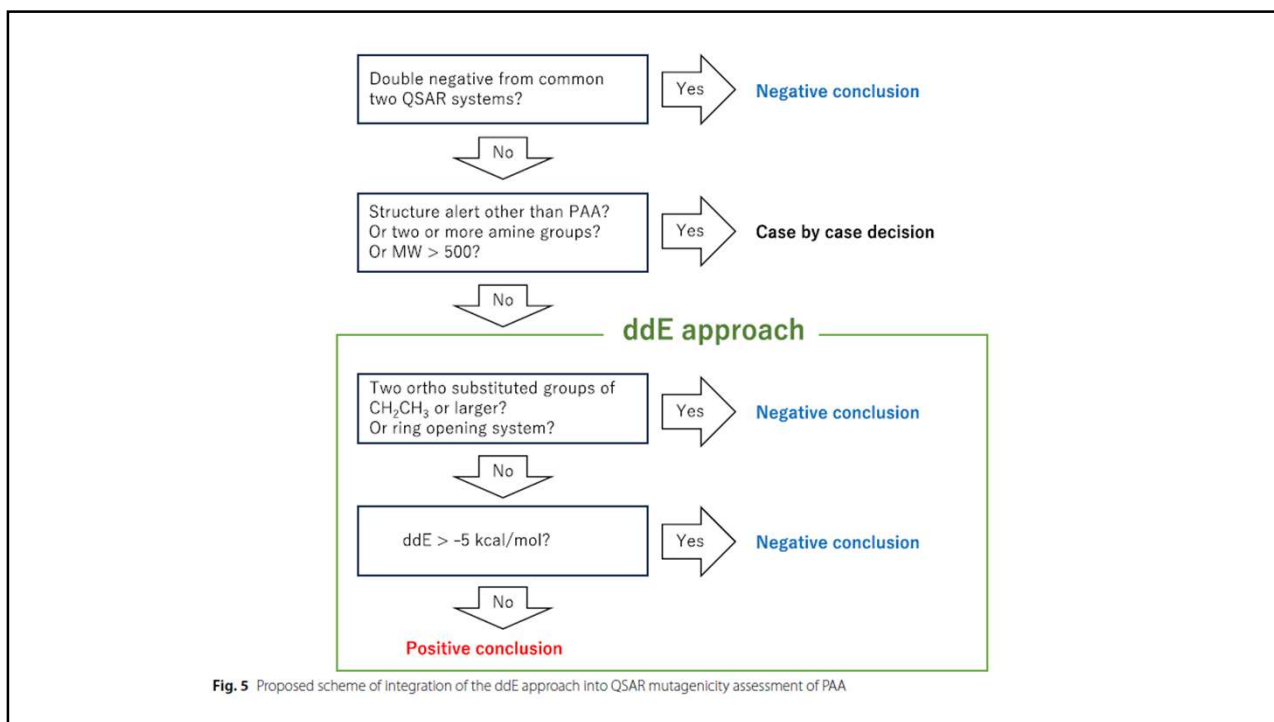
^a Sum of public and internal compounds with reliable Ames test data

^b Excluding the compounds with non-aromatic amine alerts, MW > 500, ring-opening remarks, two or more amine groups

**Fig. 4** Ames test results and ddE values of 824 PAAs in Table 6**Table 5** False positive rate of ddE based decision on PAAs with ortho substitution

R_1 <chem>NH2</chem> R_2	Example	False positive rate ^a
Class 1: two CH ₂ CH ₃ or larger substituents at both R1 and R2		88.9% (8/9)
Class 2: one CH ₂ CH ₃ or larger substituent at ortho position with and without the other ortho substitution		55.0% (44/80)
Class 3: Smaller substituents at R1 and/or R2		17.9% (5/28)
Class 4: No ortho substitution		29% (29/100)

^a -5 kcal/mol ddE cutoff



共同研究のまとめ

- アステラス製薬、EAファーマ、エーザイ、富士フイルム、JT、クミアイ化学、田辺三菱製薬、中外製薬、日本農薬、日本新薬、日産化学、小野薬品、大鵬薬品、武田薬品、帝人の15社と、厚労省がデータを提供し、合計757化合物の非公開Amesデータを利用できた。
- 選考論文よりも化合物範囲を広げて、ddEの陽性判断基準値の最適化ができた。
- 分子量とort置換基の影響を加味し、デシジョンツリーを提案した。
- 本共同研究は目的を完遂し、論文公開をもって終了した。