# [P15] How Frequently Are Pan-Assay Interference Compounds Active?

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Pan-assay interference compounds (PAINS) are small molecules that might be reactive under assay conditions and might produce false-positive assay signals, which cause substantial problems for biological screening and medicinal chemistry [1-3]. PAINS comprise a set of 480 compound classes originally identified in AlphaScreen assays that are typically contained as substructures in larger compounds [1]. Computational filters encoding PAINS can be used to detect compounds with potential chemical liabilities that require follow-up analysis [4]. Such filters are controversially viewed in the field [5] but provide first-path alerts for potential liabilities. Undetected interference compounds often propagate through medicinal chemistry programs and compromise their outcomes [3]. Interference characteristics of PAINS have been computationally investigated by systematically analyzing publicly available screening data and determining activity profiles of screening compounds with PAINS substructures [5,6]. In our study [6], ~23,000 extensively tested compounds containing 270 PAINS substructures were detected and their hit rates determined. Many compounds containing PAINS substructures were found to be consistently inactive in all assays they were tested in. Hit rates of PAINS varied but were often low, with median values of two to five hits for compounds tested in increasing numbers of assays. Only small subsets of compounds produced an abundance of hits. Furthermore, the same PAINS substructure was often found in consistently inactive and frequently active compounds, suggesting that the structural context in which PAINS are presented plays an important role for interference potential [6]. To support further analyses of PAINS, 270 PAINS substructures contained in extensively assayed compounds and their activity profile statistics have been made freely available as an open access deposition [7].

Bibliography:

[1] J. B. Baell; G. A. Holloway. J. Med. Chem. 53 (2010) 2719−2740.
[2] J. B. Baell; L. Ferrins; H. Falk; G. Nikolakopoulos. Aust. J. Chem. 66 (2013) 1483-1494.
[3] J. Baell; M. A. Walters. Nature. 513 (2014) 481-483.
[4] S. Saubern; R. Guha; J. B. Baell. Mol. Inf. 30 (2011) 847-850.
[5] S. J. Capuzzi; E. N. Muratov; A. Tropsha. J. Chem. Inf. Model. 57 (2017) 417-427.
[6] S. Jasial; Y. Hu; J. Bajorath. J. Med. Chem. 60 (2017) 3879-3886.
[7] https://www.zenodo.org/record/557207.