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KAOS-Kinases automated outlier searcher for cancer drugs target discovery

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Mining kinases expression levels in a set of tumor cell lines has a great relevance in the early stage of drug development process in order to identify candidate therapeutic targets to be tested against in-house available compounds. The identification of a tissue specific kinase over-expression, indeed, may suggest an underlying genomic arrangement which can be further investigated as the causal mechanism of cancerogenesis, thus indicating potential new drug targets. In order to achieve this goal, we developed KAOS (Kinases Automated Outlier Searcher), a software engine aimed at the identification of kinases which are over-expressed in a particular tissue. KAOS implements the following automated strategy: i) tissue annotation for the whole cell line dataset, ii) identification of outliers for each tissue-specific distribution, by the Grubbs test for outliers, iii) applies a chain of filtering criteria to isolate tissue-specific outliers (minimal expression threshold, distance from the 75th percentile of the tissue-specific distribution, comparison of the number of outliers against the whole dataset), iv) provides a graphical resume of the most relevant outliers and related gene expression distributions. The method effectively found well known tissue-specific overexpression, such as RET in TT thyroid papillary tumor cell line, as well as ROS1 in glioblastoma (MG-138) and lung tumor (HCC-78) cell lines. Finally, KAOS represent a concrete proof-of-concept of how the overwhelming availability of genomic knowledge bases, which are still grow over time, may be a great source of data to be exploited for early discovery, even before planning in-house experimental efforts.

Biography

Angelo Nuzzo has completed his Ph.D. in Bioengineering and Bioinformatics at the University of Pavia, Italy, and postdoctoral studies within an international joint project between the same University, the University of Ljubljana, Slovenia, and the Baylor College of Medicine, TX, USA, as well as visiting researcher at the University of Florida, USA. He is currently a Bioinformatics Senior Scientist at Nerviano Medical Sciences, the largest R&D oncology-focused company in Italy. He is member of the leading International Scientific societies in the Biomedical Informatics community and author of more than 40 contributions to peer review journals and international conferences.

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