TITLE

Towards an integrated interactive database for the search of stratification biomarkes in Alkaptonuria

AUTHORS

Cicaloni V[1], Rossi A[2], Zazzeri M[2], Zugarini A[2], Santucci A[1], Bernini A[1], Spiga O[1].

[1] Dipartimento di Biotecnologie, Chimica e Farmacia. Università degli Studi di Siena

[2] Dipartimento di Ingegneria dell'Informazione e Scienze matematiche. Università degli Studi di Siena

ABSTRACT

MOTIVATION Alkaptonuria (AKU) is a rare and genetic disease which causes discoloration of bone (a process called 'ochronosis') and induces early-onset osteoarthritis. AKU data have not been organized yet and the disease has no approved biomarkers. The ability to collect, integrate and analyze relevant data streams is the core for developing a "Precision Medicine Ecosystem" AKU-dedicated in which biological resources are shared between researchers, clinicians and patients. Computational modeling can be a useful guide to generate an exhaustive and dynamic picture of the individual and to identify the molecular interactions between biomarkers on which progressive diseases are based.

METHODS It has been built a new integrated interactive database thanks to MySQL, the most frequently chosen for use in web applications. In addition, data are statistically analyzed by R software (www.r-project.org) based on Pearson's correlation coefficient and P value. For a biological interpretation of statistic results, Stitch (Kuhn M. et al, 2007) and KEGG (Kanehisa M. et al, 2000) are used.

RESULTS For Precision Medicine (PM) application to AKU, the collection of as much data as possible Alkaptonuria affected patients has been needed in order to organize them in an interactive and integrated database and to find a data-processing system for AKU biomarkers discovery. The database is an effective tool for registered researchers, clinicians and patients who could both easily access all the current information, as well as being able to insert new data, refreshing or replacing previous entries. Data are divided into different sections: genetic, proteic, biochemical, histopathologic and clinical. As far as data analysis is concerned, it has been developed an algorithm to build up a refreshable correlation matrix based on Pearson's correlation coefficient and P value which allows the monitoring of renewable correlations between the most recent data

inserted. Together with the mathematical and statistical interpretation, a biological explanation of the results is needed in order to investigate on AKU biomarkers. This dynamic tool could be useful for biomarkers investigation also in other osteoarticular diseases and it is a good starting point for the creation of data management and analysis model appropriate for PM. Through the use of AKU-dedicated database and this innovative analytic approach, it has been possible to become aware of the failure of biomarkers clinically used and to improve the detenction of more exploitable prognostic biomarkers for a more reliable AKU patients clinical monitoring.