

BSC and IrsiCaixa create bioinformatics method to predict the effectiveness of antiretroviral drugs with different HIV mutations

The method represents a step towards personalised medicine, in which treatment is determined following genetic analysis of the cause of the disease in each patient

(09/05/2016, Barcelona). - The effectiveness of antiretroviral drugs used to treat HIV (human immunodeficiency virus) is frequently affected by the virus' ability to develop genetic mutations. Barcelona Supercomputing Center (BSC) and IrsiCaixa, the Catalan AIDS Research Institute, have developed a bioinformatics method to predict the effect of each mutation on the resistance of the virus to such drugs. An article published in the *Journal of Chemical Information and Modeling* explains how this method has effectively predicted the resistance of the virus with genetic mutations in the HIV-1 protease, a protein which is essential for the replication of the virus, to the drugs amprenavir and darunavir. The method could easily be applied to other drugs and proteins.

Currently, information obtained from other patients is used to predict the effects of HIV mutations on drug effectiveness. Built cumulatively through clinical experience, this knowledge is useful but has limitations. For example, it is unable to provide answers when the virus develops a mutation which hasn't previously been recorded. The method created by BSC and IrsiCaixa overcomes these drawbacks by providing predictions based on the characteristics of each genetic mutation and on the changes which the mutation produces in the virus' proteins which act as targets for the drugs.

The BSC-IrsiCaixa method combines HIV DNA sequencing, identification of genetic mutations, computational protein modelling and the simulation of drugs binding with the proteins of the virus. The entire bioinformatics analysis can be performed in fewer than 24 hours on relatively small-scale computing equipment available to any laboratory. One of the main features of the system is the use of PELE, a piece of software developed at BSC to predict how drugs will interact with their targets, which has been shown to have competitive advantages over commercially available software.

Web access

BSC has created an automatic platform, available for free via the web, on which researchers can enter a patient's HIV-1 PR protease genomic sequence and predict the effectiveness of prescribing the drugs amprenavir and darunavir. For the moment, these are the only predictions available, pending advances in research on the effect of HIV mutations on other proteins within the virus and interactions with other antiretroviral drugs.

An example of the personalised medicine of the future

BSC researcher Victor Guallar, who appears as principal investigator in the article published today in the *Journal of Chemical Information and Modeling* and is the lead developer of PELE, explains that 'this system is one of the first tangible steps in the area of what will eventually be personalised medicine, where treatment will be decided following genetic analysis of the causes of the disease in each patient and of which drug would be most effective in each individual case'.

'In this study we demonstrate how to connect routine clinical diagnosis of HIV-1 with structural computer modelling. This is a multidisciplinary proof of concept which overcomes the limitations of current practice when deciding antiretroviral treatment and which, in addition, allows new drugs to be designed more quickly,' adds IrsiCaixa researcher Marc Noguera-Julian, who participated in the study.

More info:

Link to the article "Computational Prediction of HIV-1 Resistance to Protease Inhibitors": <http://pubs.acs.org/doi/abs/10.1021/acs.jcim.5b00667>

Link to a video: <https://youtu.be/nRDOTloIWp0>

About BSC:

Barcelona Supercomputing Center (BSC) is the leading supercomputing centre in Spain. It specialises in High Performance Computing (HPC) and its mission is two-fold: to provide infrastructure and supercomputing services to European scientists, and to generate knowledge and technology to transfer to business and society.

BSC is a Severo Ochoa Center of Excellence and a first-level hosting member of the European research infrastructure PRACE (Partnership for Advanced Computing in Europe). BSC also manages the Spanish Supercomputing Network (RES).

The BSC consortium comprises the Spanish Ministry of Economy and Competitiveness, the Catalan Government Ministry of Business and Knowledge and the Universitat Politècnica de Catalunya – BarcelonaTech.

About IrsiCaixa:

IrsiCaixa, the Catalan AIDS Research Institute, is an internationally renowned organisation. Its objective is to undertake research on HIV/AIDS and related diseases, as well as their prevention and treatment, with the ultimate aim of **eradicating the AIDS pandemic**. It was established as a private not-for-profit foundation in 1995 by *l'Obra Social "la Caixa"*, the corporate responsibility arm of "la Caixa" bank, and the Catalan Government Ministry of Health. The centre is located at Germans Trias University Hospital in Badalona (Barcelona).

Research at IrsiCaixa is undertaken in collaboration with the most prestigious research centres in the world, and its research publications have one of the highest indices of impact factor within the field. Over 60 researchers carry out research, academic instruction and scientific dissemination at IrsiCaixa, working with health professionals and more than 3,000 patients. This model facilitates knowledge transfer between the various parties involved and enables progress towards the eradication of HIV. IrsiCaixa also participates in clinical trials to evaluate new therapeutic strategies and works in partnership with developing countries to contribute to the global fight against the pandemic.

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