EGEE NEWS RELEASE

EGEE GRID ATTACKS AVIAN FLU

During April, a collaboration of Asian and European laboratories has analysed 300,000 possible drug components against the avian flu virus H5N1 using the EGEE Grid infrastructure. The goal was to find potential compounds that can inhibit the activities of an enzyme on the surface of the influenza virus, the so-called neuraminidase, subtype N1. Using the Grid to identify the most promising leads for biological tests could speed up the development process for drugs against the influenza virus.

One of the targets of existing drugs today on the market is viral neuraminidase, an enzyme that helps the virus to proliferate and infect more cells. As this protein is known to evolve into variants if it comes under drug stress, drug resistance becomes a potential concern in case of an influenza pandemic.

The challenge of the *in silico* drug discovery application is to identify those molecules which can dock on the active sites of the virus in order to inhibit its action. To study the impact of small scale mutations on drug resistance, a large set of compounds was screened against the same neuraminidase target but with various, slightly different structures. With the results from the *in silico* screening, researchers can predict which compounds and chemical fragments are most effective for blocking the active neuraminidases in case of mutations.

The drug discovery process is being greatly accelerated by the use of the EGEE and associated computing Grid infrastructures. For the docking of 300,000 compounds against 8 different target structures of Influenza A neuraminidases, 2000 computers were used during 4 weeks in April – the equivalent of 100 years on a single computer. More than 60 000 output files with a data volume of 600 Gigabytes were created and stored in a relational database. Potential drug compounds against avian flu are now being identified and ranked according to the binding energies of the docked models.

"With the help of the high-speed computing and huge data managing capabilities of the Grid, possible drug components can be screened and studied very rapidly by the available computer modelling applications," says Ying-Ta Wu, biologist at the Genomics Research Center of the Academia Sinica in Taipei. "This will free up medicinal chemists' time to better respond to instant, large-scale threats. Moreover, we can concentrate our biological assays in the laboratory on the most promising components, the ones we expect to have the greatest impact."

"With these results, the Grid demonstrates that it is a powerful and reliable resource for scientists, opening up new research possibilities and improving existing methods," said Viviane Reding, European Commissioner responsible for Information Society and Media. "I am very

grateful to see that the European flagship Grid infrastructure is contributing to solving current and socially important problems such as avian flu."

Taking advantage of the experience acquired in the previous WISDOM data challenge on malaria, the Grid-enabled *in silico* process was implemented in less than a month on three different grid infrastructures: AuverGrid, EGEE, and TWGrid, paving the way for a virtual drug screening service at a large scale. The majority of computing is conducted on the WISDOM platform; in addition, a light-weight application framework called DIANE was also adopted in this challenge and used to perform a sizeable fraction of the total activity to enable efficient computing resource integration and usage. The next WISDOM data challenge against several targets of neglected diseases will take place in autumn 2006.

This drug discovery application against the avian flu virus was jointly deployed by the Genomics Research Center, Academia Sinica, Taiwan; Academia Sinica Grid Computing Team, Taiwan; Corpuscular Physics Laboratory of Clermont-Ferrand, CNRS/IN2P3, France; Institute for Biomedical Technologies, CNR, Italy, in collaboration with the EGEE project, the AuverGrid regional grid in Auvergne, and the TWGrid. This work took place in collaboration with the EMBRACE network of excellence and the BioInfoGrid project.

Note to Editors:

1.   To speed-up and reduce the cost to develop new drugs, researchers use *in silico* docking algorithms to compute the probability that potential drugs will dock with a target protein. *In silico* drug screening can thus accelerate the discovery of novel potent inhibitors by minimising the non-productive trial-and-error approach in a laboratory.
2.   For more information on the drug discovery application against the avian flu virus, please contact Ying-Ta Wu (GRC, Academia Sinica), email: ywu@gate.sinica.edu.tw
3.   For more information about WISDOM (wide *in silico* docking against malaria), please visit: http://wisdom.eu-egee.fr/ or contact Nicolas Jacq (CNRS/IN2P3), email: jacq@clermont.in2p3.fr.
4.   For more information about the Enabling Grids for E-sciencE (EGEE) project please see http://www.eu-egee.org/ or contact Hannelore Hammerle (CERN), EGEE External Relations Officer, telephone: +41 22 767 4176 or email: hannelore.hammerle@cern.ch
5.   For more information about DIANE (Distributed Analysis Environment), please visit: http://cern.ch/diane/
6.   For more information on the Corpuscular Physics Laboratory of Clermont-Ferrand, CNRS/IN2P3 please see http://clrwww.in2p3.fr/
7.   For more information on the Genomics Research Center of Academia Sinica, Taiwan, please see http://www.genomics.sinica.edu.tw/
8.   For more information on the Academia Sinica Grid Computing Team (ASGC), Taiwan, please see http://www.twgrid.org/
9.   For more information on the Institute for Biomedical Technologies, CNR, Italy, please see http://www.itb.cnr.it/
10.   For more information on the AuverGrid please see http://www.auvergrid.fr/
11.   For more information on EMBRACE, please see http://www.embracegrid.info
12.   For more information on the Bioinformatics Grid Application for life science (BioinfoGRID) project, please see http://www.itb.cnr.it/bioinfogrid