Amsterdam science & innovation Award 2017

Science & Business Event

Innovative ideas in Pharma & Biotech

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A new dual-action medication to cause double-trouble for Tuberculosis

Tuberculosis is once again a threat to the world, especially due to the multi-drug resistant species that have infected around 500.000 humans world-wide in 2015 only. Treatment options for these patients are limited and expensive, and more dramatically, in some cases completely absent; clinicians have no cure for these patients. Using high resolution microscopy techniques we discovered that upon antibiotic treatment the DNA of Mycobacterium tuberculosis condenses into a single clump (Figure 1).

Recovery from this condensed state turns out to be a not yet discovered weak spot of the bacteria. Importantly, by using this weak spot we could influence survival of the bacteria dramatically. This is a whole new approach in antibiotic treatment for these pathogenic mycobacteria, and as also other bacteria condense their DNA, the approach will be applicable for more pathogens.

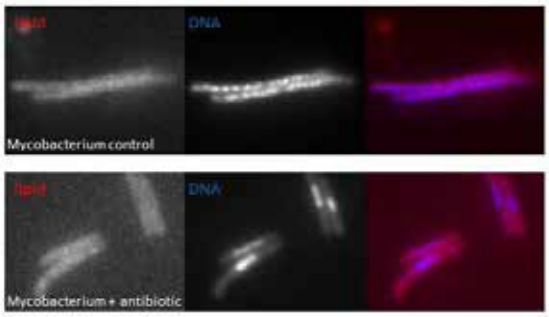


Figure 1 Mycobacteria treated with antibiotics relocate their DNA in a clump after antibiotics

The dramatic effect on the tuberculosis survival is paralleled by the simplicity of the application. We want to develop a tablet that will initially release the antibiotic in order to condense the DNA of the bacteria, and subsequently release the inhibitors affecting the recovery of the condensed state. We want to collaborate with companies to find the optimal combination and apply this new strategy in drug development to treat patients as soon as possible.

***Nicole van der Wel**, Researcher, Academic Medical Center Amsterdam*

Amsterdam young adult twins: their lives 30 year later

Between 1985 and 1988 I saw a large group of twin families from Amsterdam who were invited to take part in my PhD research project. I saw 160 identical and fraternal twin pairs and their parents from Amsterdam and looked at their lifestyle (smoking, exercise), their educational profiles, their health (blood pressure, lipid levels) and how they responded to stress. I would very much like to invite this group back. The twins were adolescents and young adults (between 13 and 18 years old) when they took part in this project.

Almost 30 years later, I would like to invite them back and look at their developmental trajectories: what do their careers look like, how is their health, did they stay in Amsterdam, did they have children themselves? With all these life outcomes, to what extent did genetic factors play a role and what other important determinants can we identify?

***Dorret Boomsma**, Researcher, Vrije Universiteit Amsterdam*

Innovative ideas in pharma & biotech

MDStudio: Molecular Dynamics workflows made easy

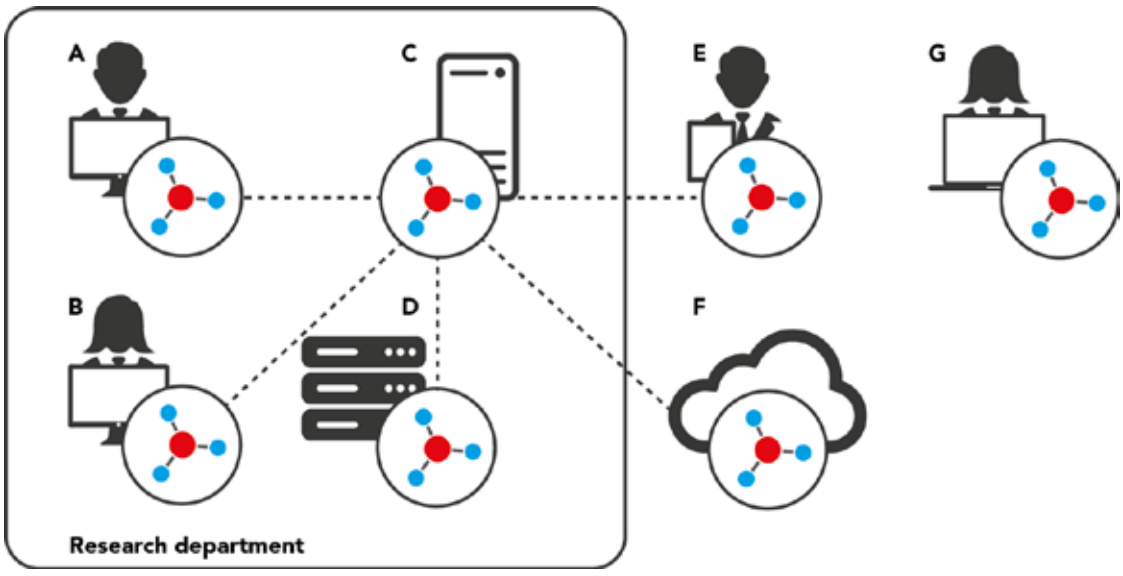
Molecular Dynamics (MD) simulations can directly aid to drug design and development, bioengineering, understanding drug resistance, or other (bio)molecular-oriented R&D.

To fill the current gap that prevents wide-spread application of MD-based methods in applied settings we have launched the MDStudio software initiative with three main ideas in mind:

(i) developing a software platform to let the user focus on science, not IT
(ii) integration of MD-based workflows
(iii) involving the community.

With MDStudio we will directly contribute to the straightforward application of MD-based methods in drug design and research. Furthermore, we envision that our platform will function as a catalyst for the further development and use of state-of-the-art MD methods in academia and industry.

MDStudio development is coordinated by Daan Geerke (PI) and Marc van Dijk (senior scientist), on the right- and leftbackcorners of the enclosed picture, which shows the Geerke group (together with collaborator Bill Swope, IBM Research).



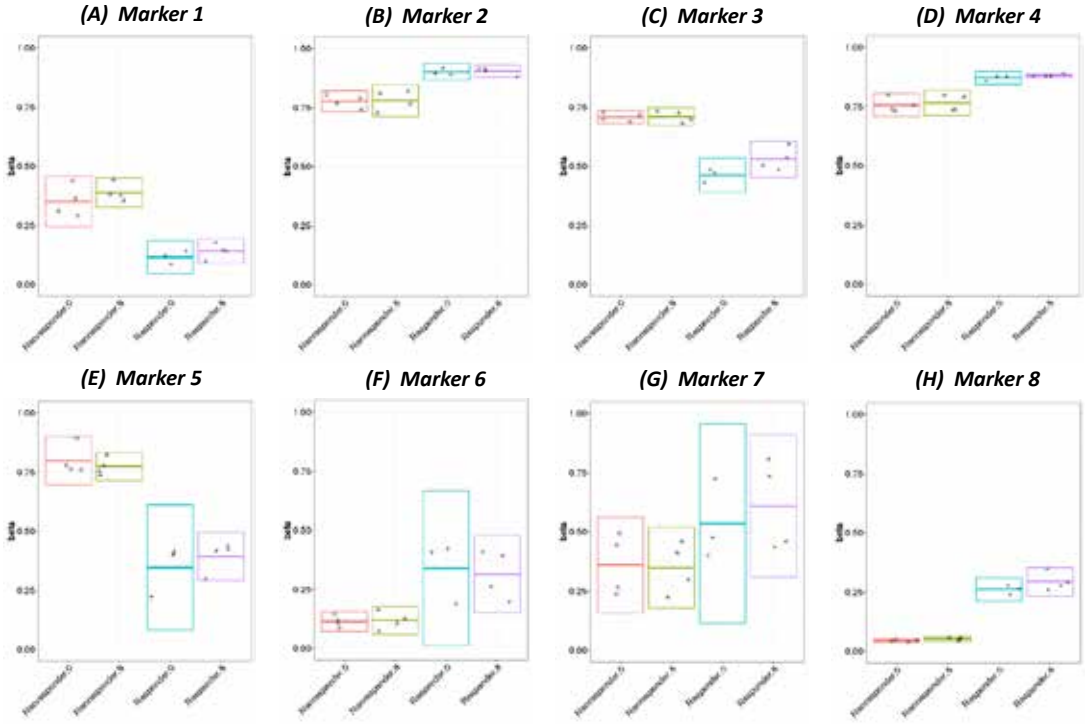
***Daan Geerke**, Researcher, Vrije Universiteit Amsterdam*
***Marc van Dijk**, Researcher, Vrije Universiteit Amsterdam*

Innovative ideas in pharma & biotech

Response or no response, that's the question!

Crohns disease (CD) is a chronic inflammatory disease, which affect the gastrointestinal tract and leads to substantial morbidity. Therapeutic intervention of CD, but also other disorders involving a hypersensitive immune system, are usually assessed as matter of trial and error. Assessing the right therapy takes for some individual cases a long period time, resulting in a dramatic course of the disease and high social and economic burden.

Recently we, Peter Henneman, geneticist and Anje te Velde, basic CD researcher, performed a pilot study in which we aimed to detect genome-wide methylation patterns in peripheral blood from CD that may predict response to anti-TNF-treatment (adalimumab). Our analysis yielded nine potential epigenetic biomarkers. To date we are setting up followup studies together with commercial and pharmaceutical companies in order to develop in a short as possible period of time a novel and cost-effective epigenetic biomarker kit that enables prediction of response to particular immunosuppressive agents/biologicals.



Legend to supplementary figures 1 A to H: Differential methylated positions (DMPs) between adalimumab responders and non-responders at both T0 and T8 yielded 8 DMPs at a Benjamin-Hochberg adjusted α of 0.05. DMPs showed a average methylation difference of at least a 10%, the largest effect size observed was a methylation difference of 41% (E). X-axis, classification of responders and non-responders at time point 0 and 8 weeks. Y-axis, DNA-methylation level expressed as beta-values, i.e. 0-100% methylated.

***Peter Henneman**, Researcher, Academic Medical Center Amsterdam*
***Anje te Velde**, Researcher, Academic Medical Center Amsterdam*

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Treatment of sepsis 2.0

The presence of pathogens in the bloodstream can cause the onset of sepsis or even septic shock due to the patient's own immune response. One of the mechanisms to protect the host from such blood-borne infections is immune adherence clearance (IAC), the process by which pathogens are bound by red blood cells (RBC) and transported to the liver and spleen where they are engulfed by macrophages. Furthermore, we found that these RBC-pathogen complexes can be specifically depleted by a commonly used filter, which provides a novel generic therapy for patients suffering from sepsis. We foresee that the use of a so-called apheresis device, which separates one particular constituent of blood and returns the remainder to the circulation, can be used to treat septic patients. Of importance, we have constructed a prototype of such an apheresis device which is indeed effective in depleting red blood cellpathogen complexes from blood.

Immunology

Sanquin
Blood Supply

Treatment of sepsis through depletion of red blood cell/pathogen complexes.

Michiel Blankenvoorde, PhD Business Development Manager
Robin van Bruggen, Group Leader Red Blood Cell Research, Department of Blood Cell Research

RESEARCH | DIAGNOSTICS | PHARMACEUTICALS

***Robin van Bruggen**, Sanquin*