CIC biomaGUNE: CIF: G-20788840· Parque Tecnológico de San Sebastián · Pº Miramón 182· 20014 San Sebastián (Gipuzkoa)· Tel.: + 34 943 00 53 00· Fax: + 34 943 00 53 01· info@cicbiomagune.es ·www.cicbiomagune.es

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seminar

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**Seminar Room**

*Host: Dr. Niels Reichardt*

# Engineering of a gene therapy viral vector surface as plataform to generate chimeric vectors with new properties

*Dr. Rafael Aldabe Arregui*
*Gene Therapy of Renal Diseases and the Study of*
*N-terminal Acetylation of Proteins Group*
*CIMA. University of Navarra*

In vivo gene therapy has started to give solution to genetic diseases like haemophilia. Moreover, there are many gene therapy treatments in clinical trials treating different genetic diseases without any therapeutic treatment nowadays. However these vectors present some limitations like limited tropism, sensitivity to preexisting circulating anti-AAV neutralizing antibodies, unsatisfactory potency, … that are making necessary the use of high doses of the therapeutic vector. Clinical trials increasingly report adverse events in cohort of patients injected with the highest rAAV doses. With the development of more effective viral vectors therapeutic thresholds could be reached with lower vector doses, thereby improving targeting potential and reducing the likelihood of the aforementioned adverse events.

The most common strategy to optimize rAAV vector efficacy involves modification of the viral capsid via genetic engineering, using either rational design or directed evolution approaches. Although these strategies are promising, manufacture of new modified rAAV vectors is challenging, as it requires optimization of each stage of the production and purification processes, as well as complex characterization of the newly generated particles. Another possibility is a chemical engineering approach to rAAV vector optimization based on the presence of specific reactive non-natural amino-acids on the AAV capsid that allow click-chemistry reactions to link different moieties that can provide new properties to the viral particle.

We have identified several residues on the AAV9 capsid that can be substituted by and azido-lysine without affecting recombinant viral particles production. We have used these residues to attach glycans to the AAV surface without interfering with viral infectivity in cell culture. We have started to explore the effects of these modifications on AAV viral infectivity in vivo.