U E A A NEWSLETTER

2022, N° 4

Tbilisi, 29 April 2022

Latest News

Considerations on gene editing application in livestock animals
from the Italian Animal Science and Production Association (ASPA)

A peculiarity of gene editing (GE) in animals, compared to applications in plants, is the mandatory requirement of taking into account its effect on the animal welfare, as well as on the safety of the produced food that is produced.

- GE applications that introduce variants of important effect (in major genes) and that have been already "tested" within the target or in neighboring species and for which positive and negative effects are already known, are to be considered safe. Examples are the mutations in the myostatin gene in beef cattle (positive aspects: greater feed efficiency, leaner meat, higher yield at slaughter; negative aspects: greater difficulty in calving) or mutations in the prolactin receptor that induces the SLICK phenotype (positive aspects: tolerance to high temperatures, stress reduction and maintenance of production at high values of THI). In both cases, animal products derived from animals carrying these mutations have been consumed by humans for decades without negative consequences.

- **The goal** of gene editing should however be to increase the efficiency of production while maintaining or improving the animal welfare (e.g. SLICK mutation, or in genes that increase resistance to diseases and parasites) and the sustainability of animal productions (e.g. decreasing methane emissions from ruminants if ever an interesting mutation is found). Increased production levels coupled with increased animal stress would lead to negative outcomes for the farmers and for the community.

- **The efficacy** of the technology should be also carefully considered. It is not certain that the inclusion of a variant in a genetic background (i.e. in a breed) different from that in which the mutation was found, has the same effect. In mice there are cases in which knock out of myostatin did not give hyperplasic phenotype,

- **Appropriate strategies** to implement effectively the GE intervention at the population level should be designed. The new variant must be disseminated through a careful plan that controls inbreeding.

- **Gene editing technologies** based on TALENS' or CRISPR-CAS appear to be highly precise and reliable. Few "off-target" events have occurred in many experiments, sometimes none. Possible to identify off-target events by full genome sequencing. Expensive because high sequence reliability is required, hence deep sequencing (many Xs). Assessing possible effects of off-target mutations is still problematic despite genome annotation efforts. The Human Encode project found that at least 60% of the genome is transcribed and that many untranslated RNAs have regulatory function.

- **As a general consideration**, gene editing is certainly a very useful technology in the animal sector right now at research level to test the effect of gene variants in in vitro systems (cells, embryos). Thinking about possible application in animal breeding, the priority is the search for variants that are worth introducing in cosmopolitan breeds through GE. These variants must have the characteristics mentioned before regarding effect, efficiency, welfare, environmental impact. They are likely to be found in local breeds, to be characterized before losing them. For now the number of candidate variants for zootechnical applications is really limited. Different is the discourse for applications in the biomedical sector (disease models, humanized organs), but that is out of our context.