

Animal welfare: optimization of an *in vitro* test alternative to that in animals for the control of vaccine batches.

An *in vitro* method for vaccine batch release can be a valid alternative to the test currently carried out in animals. In particular, the monocyte activation test (MAT) allows the detection of pyrogens, molecules able to induce unwanted febrile processes.

Development and optimization of this test were carried out by a team of Istituto Superiore di Sanità (ISS) researchers thanks to Innovative Medicine Initiative funding as part of "Vaccine batch to vaccine batch comparison by consistency testing ["VAC2VAC"](#) project. These data have been recently published in [ALTEX](#) journal.

"This method is a valid alternative to the pyrogen test currently carried out in rabbits - declares **Elia M. Coccia**, researcher of the Immunology Unit in the Department of Infectious Diseases (ISS), head of the research team - and is, therefore, in line with the Directive 2010/63/EU on the protection of animals used for scientific purposes. In particular, in the MAT assay vaccines are directly tested on cultures of human monocytes present in the peripheral blood, which represent the main cells able to detect pyrogens. These cells release factors that induce inflammation, thus causing fever, such as interleukin 6 (IL-6), IL-1 β and tumor necrosis factor alpha (TNF- α). By detecting their presence, it is therefore possible to establish whether there are pyrogens in the vaccine under testing."

"In the study, MAT was optimized to evaluate the pyrogenic content of the human vaccine against tick borne encephalitis - continues the expert - but its application can potentially be extended to many other vaccines for human use."

"The added value of this assay - specifies **Marilena P. Etna**, researcher of the ISS team – relies on the possibility to detect pyrogens in vaccines intended for humans on a platform based on human cells that have a more accurate sensitivity and a more suitable in respect to rabbits".

"In this context - concludes **Elia M. Coccia** - thanks to the experience gained with the development of the MAT test, ISS is among the few Official European Control Laboratories that are currently able to perform this test, promoting and actively contributing to the development of alternative strategies to the use of animals".

This work was carried out in collaboration with **Christina von Hunolstein** and **Andrea Gaggioli** of the National Center for Control and Evaluation of Drugs (ISS).