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Molecular Medicine Communications

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Editor's Choice

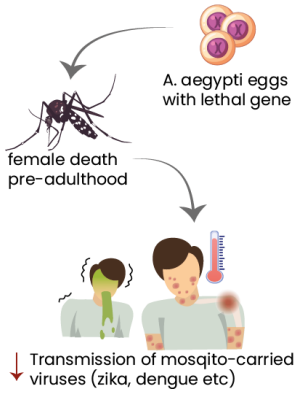
Editor's Selection of the Important Research Investigations in the Field of Molecular Medicine Communications from Around the World

Editorial Staff

Fighting Mosquitoes with Mosquitoes

(doi.org/10.55627/mmc.002.001.0078)

A first of its kind open-air study of genetically engineered mosquitoes has been conducted by scientists in the US. The biotechnology company Oxitec, spear heading these experiments, claim to have obtained positive results.

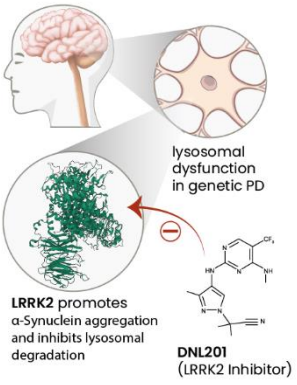


However, much more elaborated and intricate studies are needed to establish whether these mosquitoes can suppress a wild population of mosquitoes that serve as viral carriers for chikungunya, dengue, Zika and yellow fever. The study has been green lit since April 2021, and is underway in the Florida Keys which are group of tropical islands in the southern tip of Florida. Over the course of seven months, approximately 5 million genetically engineered *Aedes aegypti* mosquitoes were released by Oxitec and the firm has now completed the evaluation of almost all the release sites. The firm which is situated in Abingdom, United Kingdom showcased their results in a webinar on April 6th but are yet to publish. About 22,000 eggs were captured and taken back to the labs for observational hatching. Oxitec claims that all the female mosquitoes harboring the lethal gene died prior to adulthood. ***Nature*** 604, 608-609 (2022)

A New Target for Parkinson's Disease

(doi.org/10.55627/mmc.002.001.0079**)**

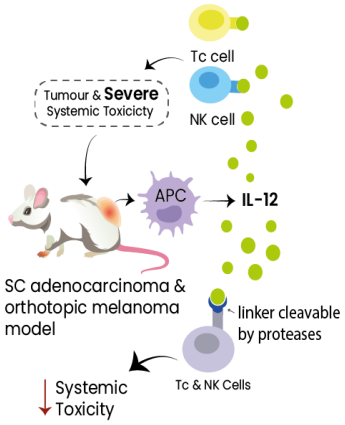
LRRK2 blockade has emerged as potential target for developing disease-modifying therapies against Parkinson's disease.



Both in cellular and animal models, DNL201- a first-in-class central nervous system–penetrant LRRK2 kinase inhibitor, successfully mitigated the LRRK2 function resulting in re-establishing lysosomal activity as per the findings of Jennings and colleagues. In both healthy volunteers and patients with Parkinson's Disease, LRRK2 kinase was inhibited by DNL201 and the drug candidate was also shown to be safe and tolerable at doses which improved lysosomal functioning. These finding argue for advanced studies on LRRK2 inhibitors including early as well as late-stage clinical investigations in patients with Parkinson's disease. ***Sci. Transl. Med***.14, eabj2658 (2022).

A Checkpoint for Systemic Toxicity (doi.org/10.55627/mmc.002.001.0080)

Cytokines such as interleukin 12 (IL-12) possess myriads of functions in modulation of immune responses but despite having significant therapeutic potential they can also stimulate toxic activation of immune cells.

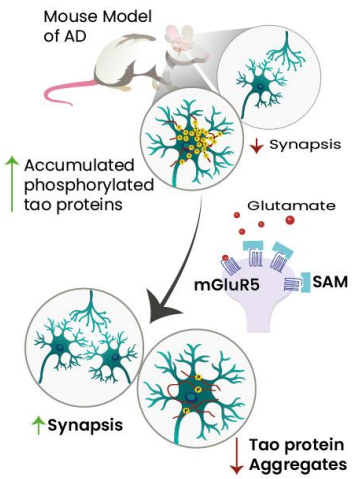


In a study by Mansurov and colleagues, the pleiotropic effects of IL-12 were successfully prevented by attaching the cytokine to a genetically engineered fragment of IL-12 receptor and allowing the complex to be processed by tumor-associated proteases. Subsequently, when injected into cancer-containing mice, IL-12 was only activated in the tumor microenvironment. Upon administration, systemic toxicity was not observed while the masked IL-12 was able to stimulate immune cells and the tumors responded to immune checkpoint therapy. This methodology could be suitable to curate more cytokines as therapeutic agents for multiple pathologies that are related with immunological demodulations without having systematic toxicity. ***Nat. Biomed. Eng***. 10.1038/s41551-022-00888-0 (2022).

A Silent Allosteric Modulator (doi.org/10.55627/mmc.002.001.0081)

Deterioration in cognitive dysfunction in Alzheimer's disease (AD) patients is associated with microglia mediated synaptic destruction. Using AD mouse models Spurrier and colleagues discerned the function of the metabotropic glutamate receptor 5 (mGluR5) on synaptic loss and demonstrated that a silent allosteric modulator (SAM) of mGLuR5 when given through the oral route successfully restored synaptic density and reduced phosphorylated TAU accumulation. The treatment in AD mice with SAM reversed the induced changes as a result of altered gene expression and blocked the synaptic confinement of the C1q complement protein. The findings of this study suggest that targeting mGluR5 with SAMs could be a powerful strategy for restricting AD-related

synaptic loss. ***Sci. Transl. Med***.14, eabi8593 (2022).



SARS-CoV-2 Shedding Shows Huge Interindividual Variation (doi.org/10.55627/mmc.002.001.0082**)**

Significant disparities in the infective potential of SCOVID-19 patients have been observed in a study conducted at a university center. Providing possible insight into superspreading events — a large population infected by a few individuals— the study provides a possible explanation of why such events play a disproportionately big role in the spread of the disease.

In their study, from late 2020 to early 2021, during the advent of Alpha and other nSARS-CoV-2 variants, 60 unvaccinated individuals with SARS-CoV-2 were identified by Christopher Brooke at the University of Illinois at Urbana– Champaign and his colleagues. For a fortnight, they collected daily samples from mild to asymptomatic patients. They found significant disparities in the number of days for which the patients shed viruses bearing infective potential: one discharged viable virus from the nose for nine days, while nine other patients did not shed any recognizable viruses capable of causing infection during the testing period. Estimates made via statistical modelling showed that the least infectious individuals shed viruses a staggering 57 times less than the most infectious individuals.

Interindivisual Variation in SARS-Cov 2 Shedding

Their findings reveal that viral RNA load maxed a few days after in the nose than in the saliva, and became untraceable approximately 14-21 days later. ***Nature Microbiol***. 7, 640–652 (2022)

Editorial Staff