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Flies against infections: a new rapid and inexpensive treatment screening platform

The *Drosophila melanogaster*, or fruit fly, shares homology with humans in some key physiological systems and serves as an efficient model to study infections. Moreover, it is an ethical alternative to reduce the use of vertebrate animals in experimentation. Several research teams have already incorporated it as a platform to rapidly evaluate candidates against infectious agents.

At the Clinical and Experimental Microbiology Unit (UMCiE) of the Germans Trias i Pujol Research Institute (IGTP), together with the Center for Comparative Medicine and Bioimage of Catalonia (CMCiB), we have been working for years with *Drosophila melanogaster* as a model to study infections. *D. melanogaster*, also known as the fruit fly, has experimental advantages due to its short life cycle, low cost, and easy genetic manipulation. These flies share homology with humans in some key physiological systems such as the digestive or immune systems, as well as 65% homology with disease-causing genes. In addition, their use in scientific research helps us reduce the use of vertebrate animals in experimentation, offering an ethical alternative for basic research.

In this context, we wanted to evaluate *D. melanogaster* as a model to study the efficacy and toxicity of new vaccines and antibiotics that have shown efficacy *in vitro* (in the laboratory),

before moving forward with studies in superior models. Recently, we have published two articles in *Frontiers in Microbiology* and *Frontiers in Immunology*, leading scientific journals in their fields. In the *Frontiers in Microbiology* article, we reviewed the infection and treatment administration techniques in the fly model, detailing how to apply them to research depending on the experimental aims. This study lays the foundation for a platform to test new drugs (Vidal, M., et al., 2024). Meanwhile, in *Frontiers in Immunology*, we focused on the innate immunity of Drosophila against infection by *Candida albicans*, a pathogenic fungus that causes severe infections in immunosuppressed patients, and analyzed how the increase in the immune response influences the evolution of the infection. We discovered that, although preimmunization helps control the growth of the yeast, it does not prevent the death of the fly, as it generates an immune storm similar to that described in some patients with COVID-19 (Cortacans, M., et al., 2024). The Drosophila model, therefore, offers us a way to design new therapeutic options not only focused on eliminating the infectious agent but also on controlling the uncontrolled immune response, which we know as "host-directed therapies". These include the use of anti-inflammatory drugs, corticosteroids, and immunosuppressants.

These publications reflect the group's maturity in the use of the Drosophila model, which has allowed us to generate an effective and low-cost platform to rapidly evaluate candidates against infectious agents, whether antibiotics or immunomodulatory drugs. This is part of our effort to reduce and replace the use of animals in research, a key objective of the CMCiB.

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