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Fri, Dec 31, 2021 at 1:09 PM

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Type of manuscript: Article

Title: Proof-of-concept preclinical use of *Drosophila melanogaster* in the initial screening of immunomodulators

Authors: Firzan Nainu *, Muh. Akbar Bahar, Sartini Sartini, Reski Amalia Rosa, Nur Rahmah, Reski Amelia Kamri, Nur Rahma Rumata, Risfah Yulianty, Elly Wahyudin

Received: 31 December 2021

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Sci. Pharm. Editorial Office <scipharm@mdpi.com>

Thu, Feb 3, 2022 at 12:12 PM

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Dear Dr. Nainu,

Congratulations on the acceptance of your manuscript, and thank you for your interest in submitting your work to Sci. Pharm.:

Manuscript ID: scipharm-1558949

Type of manuscript: Article

Title: Proof-of-concept preclinical use of *Drosophila melanogaster* in the initial screening of immunomodulators

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| Article type | Article |
| Title | Proof-of-Concept Preclinical Use of <i>Drosophila melanogaster</i> in the Initial Screening of Immunomodulators |
| Journal | <i>Scientia Pharmaceutica</i> |
| Volume | 90 |
| Issue | 1 |
| Abstract | <p>Drug discovery is a complex process, and the use of a comprehensive approach is deemed necessary to discover new chemical entities with novel mechanisms of action. This research was carried out to determine whether <i>Drosophila melanogaster</i> can serve as an appropriate model organism in the initial screening of drug candidates with immunomodulatory activities. To test this, we performed phenotypic assay and molecular analysis to investigate the immunomodulatory activities of aspirin, dexamethasone, curcumin, and epigallocatechin gallate (EGCG), that have been reported to yield such effects in the mammalian model system. In vivo survival analysis demonstrated that all drugs/compounds were relatively safe at the tested concentrations. In the infection assay, curcumin and EGCG showed a protective signature to bacterial infection in flies lacking Toll-mediated immune responses. Furthermore, dexamethasone and aspirin, drugs with immunosuppressive activity, could improve the survival of <i>PGRP-LB^A</i> mutant flies with hyperactivated immune system. These phenotypes were supported by RT-qPCR-based molecular analysis, revealing that drugs/compounds used in this study could modulate the expression level of genes related to the immune system. In conclusion, while curcumin and EGCG could promote the improvement of fly survival against infection, aspirin and dexamethasone were able to suppress overactivation of immune responses in <i>D. melanogaster</i>. These results are in line with the ones observed in the mammalian model system, further emphasizing the notion that flies would serve as a prospective model organism in the initial screening of drug candidates for their immunomodulatory activities prior to further checking in the mammalian animal models. In the end, this will reduce the use of mammalian animal models for preliminary experiments in an effort to discover/repurpose drugs with immunomodulatory activity.</p> |
| Keywords | fruit flies; immunomodulators; in vivo; drug discovery; drug repurposing |

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