# Biocompatibility of Water-Dispersible Pristine Graphene and Graphene Oxide Using a Close-to-Human Animal Model: A Pilot Study on Swine

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Graphene-based materials (GBMs) are of considerable interest for biomedical applications, and our pilot study on the toxicological and immunological impact of pristine graphene (GR) and graphene oxide (GO) using swine as a close-to-human provides valuable insights. First, *ex vivo* experiments were conducted on swine blood cells, then GBMs were injected intraperitoneally (i.p.) into swine. Hematological and biochemical analyses at various intervals indicated that neither GO nor GR caused systemic inflammation, pro-coagulant responses, or renal or hepatic dysfunction. Importantly, no systemic toxicity was observed. Analysis of a panel of 84 immune-related genes showed minimal impact of GO and GR. The animals were sacrificed 21 days post-injection, and transient absorption imaging and Raman mapping showed the presence of GO and GR in the mesentery only. Histological evaluation revealed no signs of alterations in other organs. Thus, clusters of both materials were detected in the mesentery, and GO aggregates were surrounded only by macrophages with the formation of granulomas. In contrast, modest local reactions were observed around the GR clusters. Overall, these results reveal that i.p. injection of GBMs resulted in a modest local tissue reaction without systemic toxicity. Our study, performed in swine, provides essential guidance for future biomedical applications of graphene.[1]

## References

[1] Nicolussi, P.; Pilo, G.; Cancedda, M. G.; Peng, G.; Chau, N. D. Q.; De la Cadena, A.; Vanna, R.; Samad, Y. A.; Ahmed, T.; Marcellino, J.; Tedde, G.; Giro, L.; Ylmazer, A.; Loi, F.; Carta, G.; Secchi, L.; Dei Giudici, S.; Macciocu, S.; Polli, D.; Nishina, Y.; Ligios, C.; Cerullo, G.; Ferrari, A.; Bianco, A.; Fadeel, B.; Franzoni, G.; Delogu, L. G. Biocompatibility of Water-Dispersible Pristine Graphene and Graphene Oxide Using a Close-to-Human Animal Model: A Pilot Study on Swine. *Adv Healthcare Materials* **2024**. https://doi.org/10.1002/adhm.202401783.