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Beyond the CpG: an integrative approach to decoding DNA methylation in immunometabolic health

Sinke, L.J.

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BEYOND THE CPG

an integrative approach to decoding DNA methylation in immunometabolic health

1. Meta-analysis of large-scale blood-based datasets can reveal biologically meaningful DNA methylation, even for traits non-hematopoietic in origin (**this thesis; Hannon *et al.* *eLife*, 2021**).
2. Only by triangulating evidence from complementary techniques can we extract the most promising loci from high-dimensional results (**this thesis; Gutierrez *et al.*, *Eur J Epidemiol*, 2025**).
3. CpGs should not be interpreted independently of the regulatory proteins they encounter, their broader chromatin environments, or the cells they were discovered in (**this thesis; Machado *et al.* *Brief Funct Genomics*, 2014; Schübeler, *Nature*, 2015; Yin *et al.*, *Science*, 2021**).
4. With an unprecedented wealth of public data at our fingertips, progress now depends on our ability to translate associations into clinically relevant results (**this thesis; Jiang *et al.* *Nat Rev Cancer*, 2022; Singh *et al.* *Adv Protein Chem Struct Biol*, 2024**).
5. Following robust identification of disease-associated CpGs across tissues and studies, our focus must shift from discovery to mechanistic interpretation (**Kaluscha *et al.*, *Nat Genet*, 2022; Hawe *et al.*, *Nat Genet*, 2022**).
6. Novelty accelerates science as long as fundamental questions remain at the steering wheel (**Cohen, *eLife*, 2017; Teplitzkiy *et al.*, *Proc Natl Acad Sci*, 2022**).
7. Advances in infrastructure and accessible tools now support collaborative discovery across sensitive data without compromising privacy (**Teo *et al.*, *Cell Rep Med*, 2024; The Galaxy Community, *Nucleic Acids Res*, 2024**).
8. Even the most sophisticated algorithms cannot rescue a flawed experimental design (**Leek *et al.*, *Nat Rev Genet*, 2013; Goh *et al.*, *Trends Biotechnol*, 2018**).
9. While discovery charts our scientific paths, it is the people who nurture our creativity and curiosity that illuminate them.
10. Humans are emerging as an unparalleled model organism for studying human biology.