Harnessing Epigenetics and Antimicrobial Peptides to Enhance Innate Immunity

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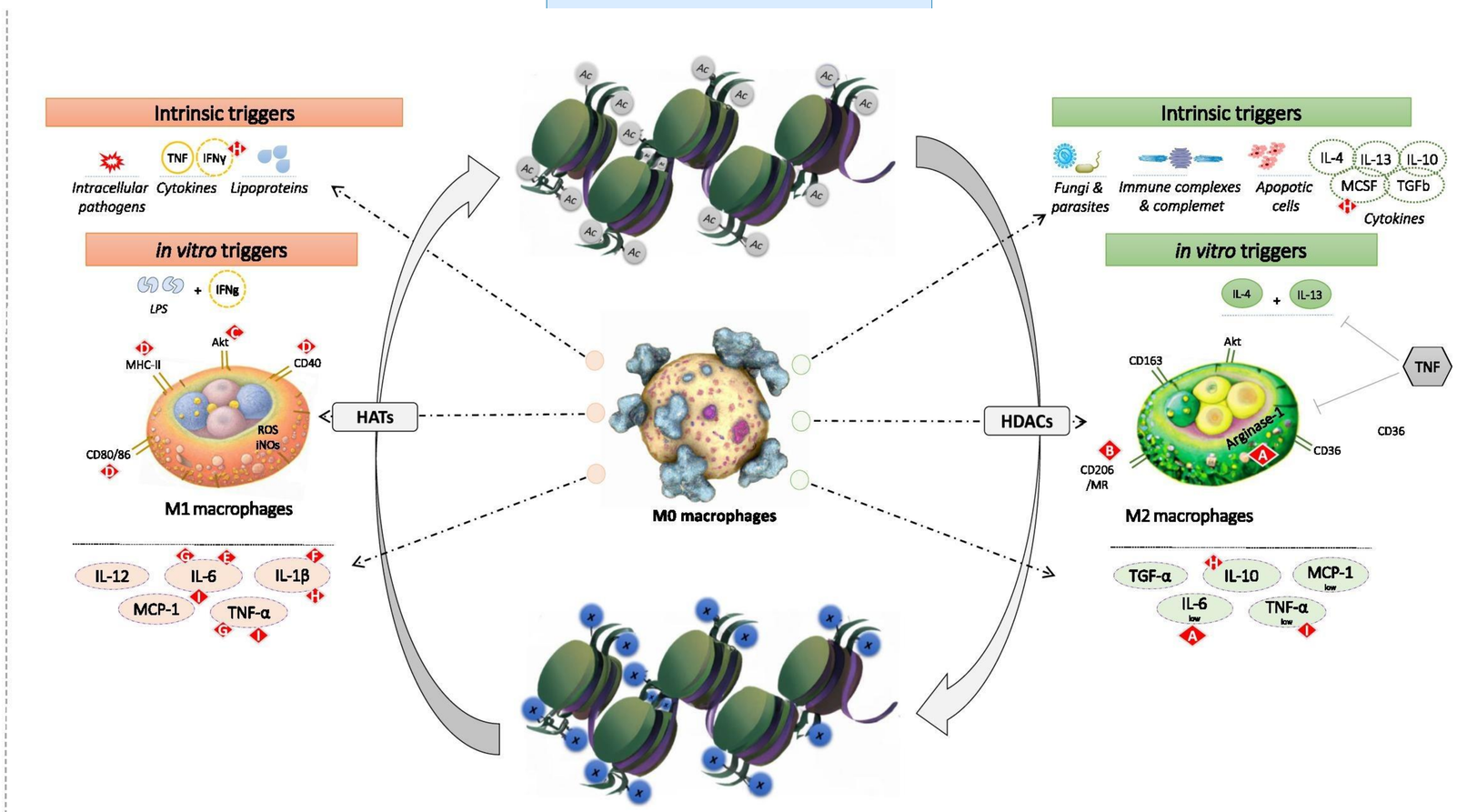
ABSTRACT

Innate immunity is the first line of defense against infections, with macrophages playing a key role through their polarization into pro-inflammatory (M1) or anti-inflammatory (M2) phenotypes. This balance dictates immune activation or suppression. Recent research highlights the role of epigenetic modulators, such as histone deacetylase (HDAC) inhibitors (HDACi), in shaping macrophage responses to infections. In addition, **antimicrobial peptides (AMPs)**— natural defense molecules with potent antimicrobial and immunomodulatory properties—are gaining attention as **crucial players in immune regulation**. AMPs not only directly combat pathogens but also **influence macrophage function**, enhancing immune responses. This review explores the impact of HDACi and other epigenetic modulators on **macrophage polarization** in diseases with strong immune components. Specific HDACs, including HDAC1, HDAC2, HDAC3, HDAC6, and HDAC8, regulate the M1/M2 balance, offering potential therapeutic targets. By **integrating epigenetic regulation** with **AMP-based strategies**, we can develop innovative approaches to **strengthen innate immunity**, particularly against drug-resistant infections.

OVERVIEW



A. Butyrate

IC_{50}
HDAC1 ~ 0.3 mM
HDAC2 ~ 0.4 mM
HDAC7 ~ 0.3 mM

B. Trichostatin A (TSA)

IC_{50}
HDAC1 ~ 0.006 μM
HDAC3 ~ 0.300 μM
HDAC4 ~ 0.038 μM
HDAC6 ~ 0.007 μM
HDAC8 ~ 0.300 μM

C. Scriptaid (SCR)

IC_{50}
HDAC1 ~ 0.3 μM
HDAC2 ~ 1.2 μM
HDAC3 ~ 1.0 μM
HDAC8 ~ 0.3 μM

D. Valproic acid

IC_{50}
HDAC1 ~ 0.7 mM
HDAC2 ~ 0.8 mM
HDAC3 ~ 1.0 mM
HDAC4 ~ 1.5 mM
HDAC5 ~ 1.0 mM
HDAC7 ~ 1.3 mM

E. Givinostat

IC_{50}
HDAC1 ~ 0.2 μM
HDAC2 ~ 0.3 μM
HDAC3 ~ 0.2 μM
HDAC8 ~ 0.8 μM
HDAC5 ~ 0.5 μM
HDAC7 ~ 0.5 μM

F. DHOB

IC_{50}
HDAC1 ~ 10 μM

G. Entinostat

IC_{50}
HDAC1 ~ 0.5 μM
HDAC3 ~ 1.7 μM

H. Vorinostat (SAHA)

IC_{50}
HDAC1 ~ 0.01 μM
HDAC3 ~ 0.02 μM

I. Ricolinostat

IC_{50}
HDAC6 ~ 0.005 μM

Conclusion

- Histone acetylation and deacetylation regulate macrophage polarization, **influencing immune responses**, inflammation, and **antimicrobial peptides (AMPs) production**.
- Targeting HDACs with chemical inhibitors can modulate macrophage function and AMP expression, **offering potential therapeutic strategies for infections** and inflammatory diseases.

References

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IN-ARMOR

THERAPEUTIC EPIGENETIC ENHANCEMENT OF INNATE IMMUNITY TO EFFECTIVELY COMBAT ANTIMICROBIAL RESISTANCE

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