P-51

Antibacterial properties of the human adipose mesenchymal stem cells-derived secretome and its protective effects at the cellular and tissue levels

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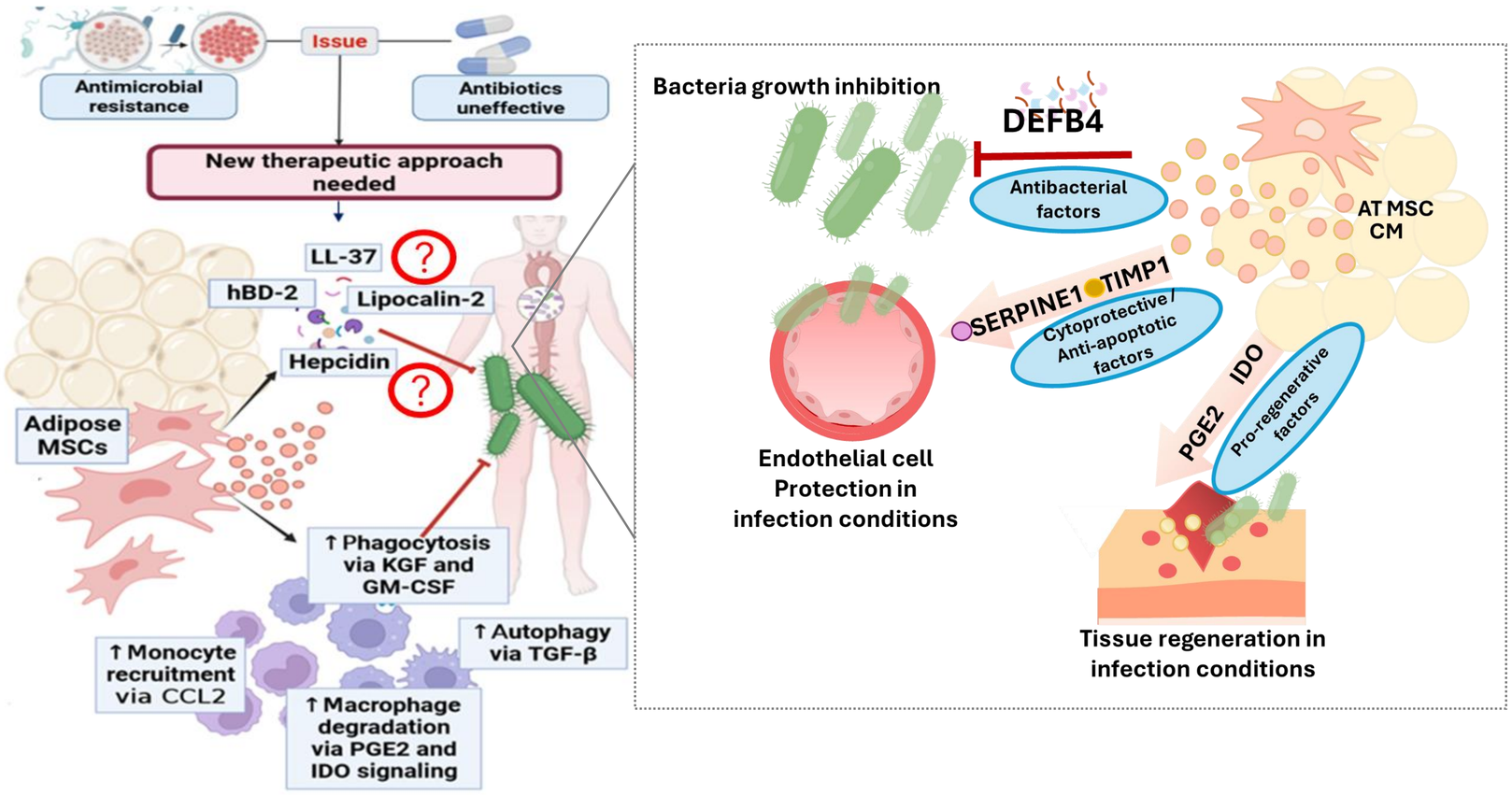
Introduction

Antimicrobial resistance (AMR) is a critical global health issue reported to cause 1.06 million deaths worldwide. The effectiveness of many conventional antibiotics is compromised by rapid bacterial mutation and increased antimicrobial resistance. This situation not only limits therapeutic options, but also jeopardizes essential clinical procedures, such as surgeries and wound healing processes, especially when resistant pathogens are involved. Adipose tissue derived mesenchymal stem cells (AT MSCs) develop within an immunological niche that potentially enhances their antibacterial activity. Moreover, their secreted factors exert immunomodulatory and regenerative effects and contain constituent peptides with antimicrobial activity, positioning them as promising candidates for antibacterial applications.



Research gap and aim

Limited number of studies have evaluated Adipose MSCs direct effects against live bacteria, and whether their cytoprotective functions are maintained in the context of active bacterial infection. In particular, the study of omentum MSs and their secreted factors are an underexplored area.

Purpose of study: To elucidate the bioactive molecules of omentum AT MSC and to determine whether they exihibit cellular and tisular protection during infection.

Methodology

In vitro antibacterial assay

Bacteria (MRSA 8r and *S.aureus N315ex*)+ CM AT MSC treatment interaction ➜ Determination of bacterial growth inhibition (CFU counts)

Cytotoxicity & co-culture

HAEC (Human Aortic Endothelial cells) + *S.aureus N315ex* + cCM AT MSC treatment ➜ Cell viability, bacterial growth inhibition (CFU counts),EC functionality and ROS production.

In vivo wound-site infection

Wound-site model (Mice) + *S.aureus* challenge + I.D. treatment➜ Macroscopic and histological changes

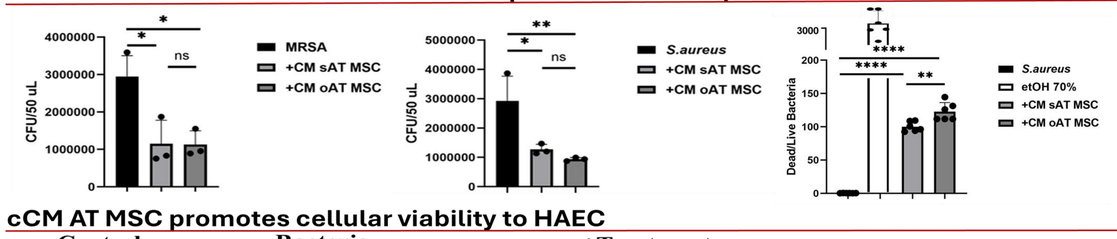
**CM AT MSC= Conditioned Medium Adipose Tissue MSCs, cCM=Concentrated Conditioned Medium , I.D.=Intradermal*

Discussion

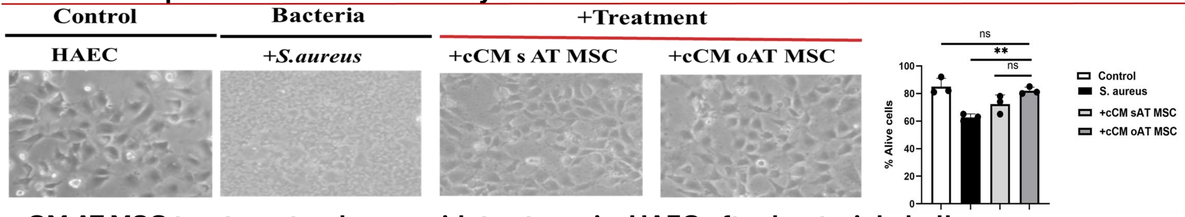
We showed the antibacterial and protective capacity of sAT and oAT MSCs-derived CM on inhibit bacterial growth while maintaining cellular integrity, as well enhancing tissular recovery in vivo. Identifying the active components provides mechanistic insight that enables future optimization using biomaterial-based platforms for clinical translation.

Results

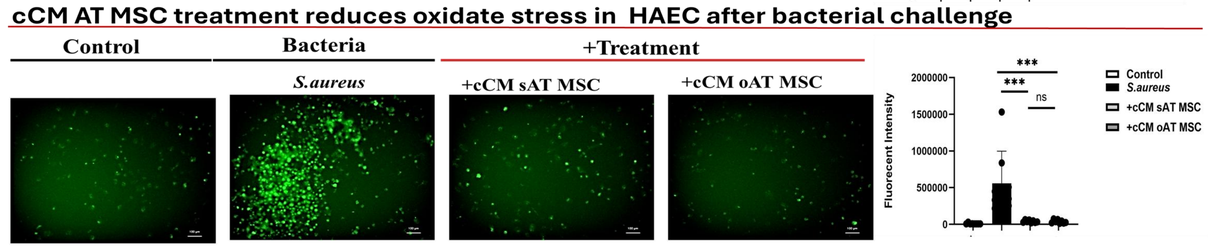
CM AT MSC reduced MRSA and *S.aureus* proliferation and permebilized bacterial membrane



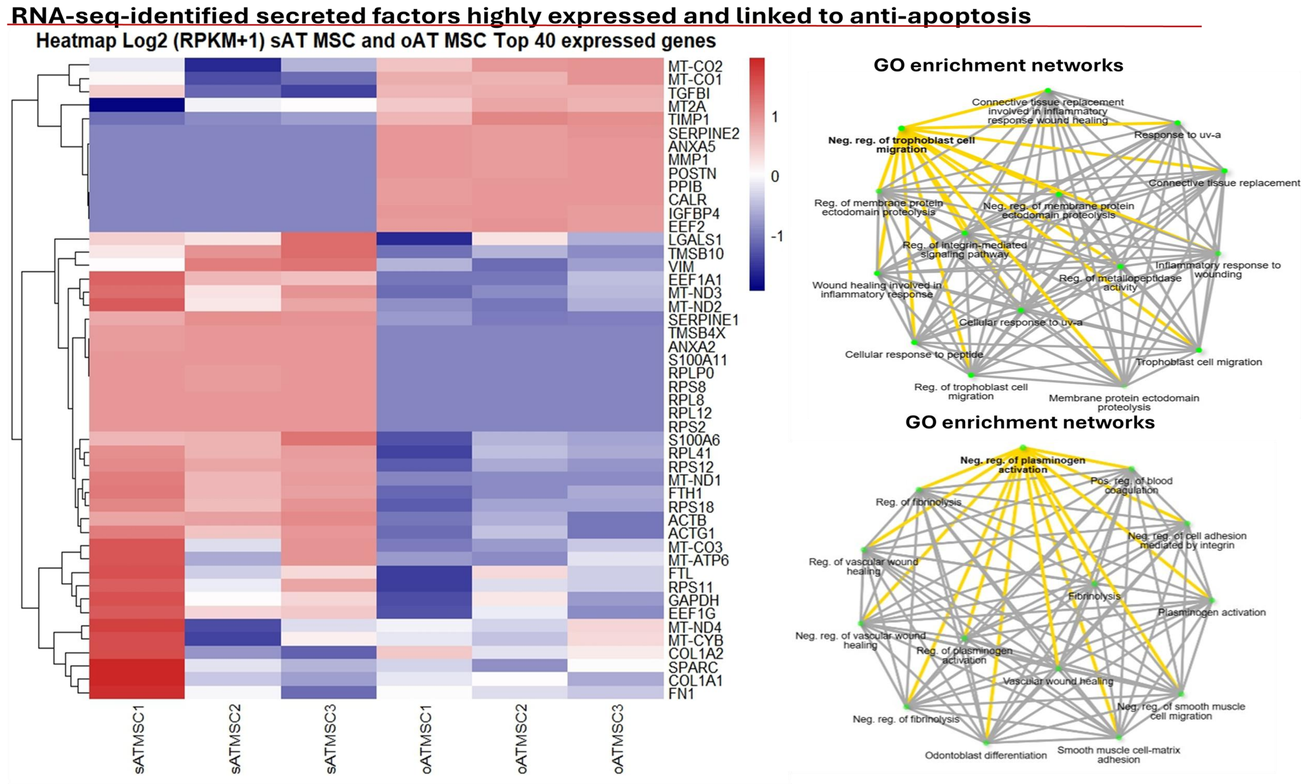
cCM AT MSC promotes cellular viability to HAEC



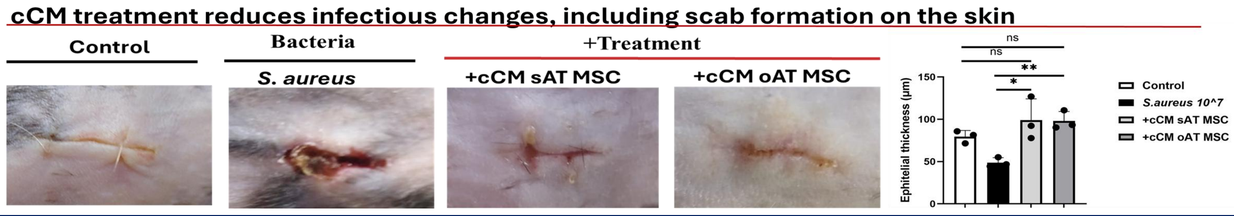
cCM AT MSC treatment reduces oxidate stress in HAEC after bacterial challenge



RNA-seq-identified secreted factors highly expressed and linked to anti-apoptosis



cCM treatment reduces infectious changes, including scab formation on the skin



Conclusion

We demonstrated previously underexplored secretory factors from adipose MSCs that drive antibacterial, protective, and regenerative actions under live bacteria infection. The identification of key factors is an important step to determine the underlying protective mechanisms and then develop tools to improve infection management in clinical practice.