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PROLONGED SURVIVAL OF E COLI BUT NOT STAPHYLOCOCCUS AUREUS IN MONOCYTES FROM PATIENTS WITH CROHN'S DISEASE

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Introduction A primary macrophage defect has been proposed to play a role in Crohn's disease (CD) pathogenesis.¹ In CD, *Escherichia coli* persist within lamina propria macrophages and peripheral blood monocytes are unable to effectively kill *E coli* in vitro.^{2,3} It is uncertain whether this abnormal bacterial handling by monocytes and macrophages in CD is limited to certain strains of *E coli* or whether a broader bacterial killing defect exists. The aim of this study was to compare intracellular survival of *E coli* with *Staphylococcus aureus* (not a usual resident of gut flora) within CD-derived and control monocytes.

Methods Peripheral blood was taken from eight healthy controls and nine CD patients. CD distribution was ileal (n=1)

and ileocolonic (n=8). Three CD patients were on thiopurines. Monocyte isolation was performed by iodixanol barrier flotation. Monocytes were challenged with a CD-derived strain of *E coli* and methicillin sensitive *Staphylococcus aureus* (MSSA). After 1 h incubation, the gentamicin protection assay was performed. Monocytes were lysed to release internalized bacteria after further incubation for 1 and 4 h. Cell lysates were plated on agar and incubated for 24 h at 37°C. Colony forming units (CFU) were counted after both 1 and 4h incubation. The CFU counts at these time points allowed relative replication to be determined.

Results Viable CD-derived *E coli* were cultured from cell lysates at 1 and 4 h from 9/9 CD patients, and in 3/8 HC's (mean increase CFUs from 1 to 4 h: CD +394%, HC -7%). Viable *S aureus* was cultured in cell lysates at 1 and 4 h respectively from 1/9 and 0/9 CD patients and 0/8 healthy controls at both time points. The difference in the number of CFU's present for each subject at 1 and 4 h was calculated and there was a statistically significant difference in mean rank of (CFU (4 h) – CFU (1 h)) between CD and HC's for *E coli* but not for staph aureus (Mann–Whitney U test).

Conclusion Within CD-derived peripheral monocytes, intracellular survival is prolonged for *E coli* but not for *S aureus*, illustrating that impairment of killing by monocytes in CD is restricted to particular bacteria. This is consistent with the clinical observation that CD primarily affects the gut which has an extensive but specific microbiome, rather than causing systemic immunodeficiency characterised by infections in other systems.

Competing interests None.

REFERENCES

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