

1 **Investigating the antagonistic activity of asymptomatic bacteriuria against uropathogenic**
2 ***E. coli*.**

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9 **Abstract**

10 Asymptomatic bacteriuria (ABU) is the presence of bacteria in urine, resembling a state of
11 commensalism. Bacteria are characterised as ABU when they have been isolated from two
12 consecutive urine samples ($\geq 10^5$ CFU/ml) from individuals, but without symptoms attributable
13 to a urinary tract infection (UTI). ABU *Escherichia coli* strains have evolved from
14 uropathogenic ancestors and lack virulence factors associated with uropathogenic *E. coli*
15 (UPEC). UPEC are the main etiological agent of urinary tract infections (UTIs), attributable to
16 $> 80\%$ of cases. The frequency at which multidrug-resistant UPEC are isolated is affecting
17 guidelines for use of former first-line antibiotics for UTIs, whereby fluoroquinolones are now
18 only recommended provided that the frequency of local resistance in UPEC is $\leq 10\%$. Bacterial
19 interference has been established against UPEC using a prototype ABU strain, *E. coli* 83972.
20 ABU strains displaying this antagonism against UPEC could be potential non-antibiotic
21 therapies for UTIs, however the mechanism behind this action is unknown. This study aims to
22 screen and characterise the inhibition of UPEC by ABU isolates, and further differentiate these
23 two classes of *E. coli*. Preliminary screening assays have detected antagonism between an ABU

24 strain against an initial panel of UPEC. Further assays have unveiled this activity is potentially
25 due to the production of an antimicrobial peptide. ABU strains will be analysed for peptide or
26 bacteriocin-encoding genes following genome sequencing. Additionally, genome comparisons
27 will be conducted to differentiate between fitness factors in ABU and UPEC. Further
28 competition assays will be conducted in *in vitro* urogenital-like environments to evaluate the
29 safety and suitability as non-antibiotic therapies for UTIs.