



Transmission of antimicrobial resistance genes from the environment to human gut is more pronounced in colorectal cancer patients than in healthy subjects

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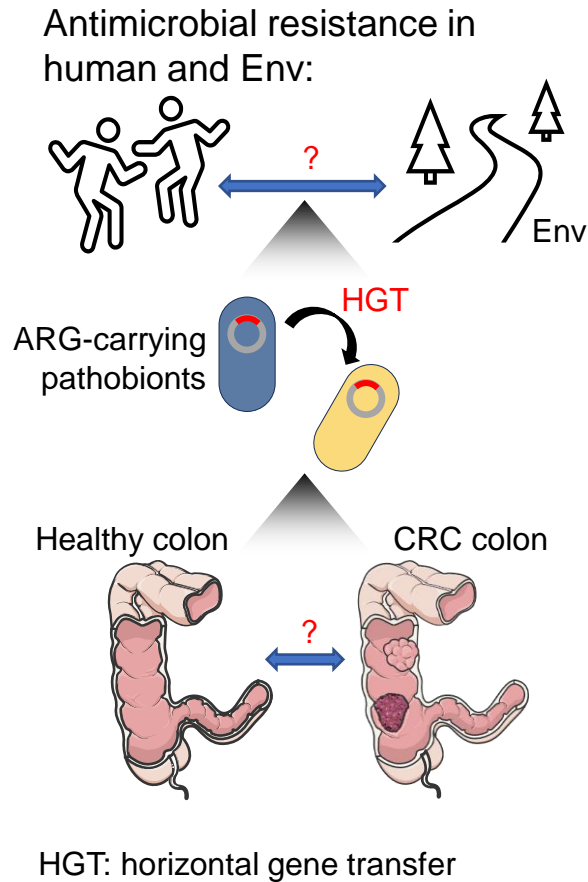
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Introduction



- Antimicrobial resistance is one of the top global public health concerns;
- Humans and their living environment (Env) are closely connected and interdependent;
- Colorectal cancer (CRC) is the second most deadly cancer worldwide;
- It is largely unclear if CRC patients have a higher carriage of antibiotic resistance and whether the abundance of antibiotic resistance genes (ARGs)-carrying gut pathobionts is increased in CRC
- Evaluating the risk of environment-gut transmission of ARGs is important to gain insights into the connectivity between the environment and human CRC

Sample collection

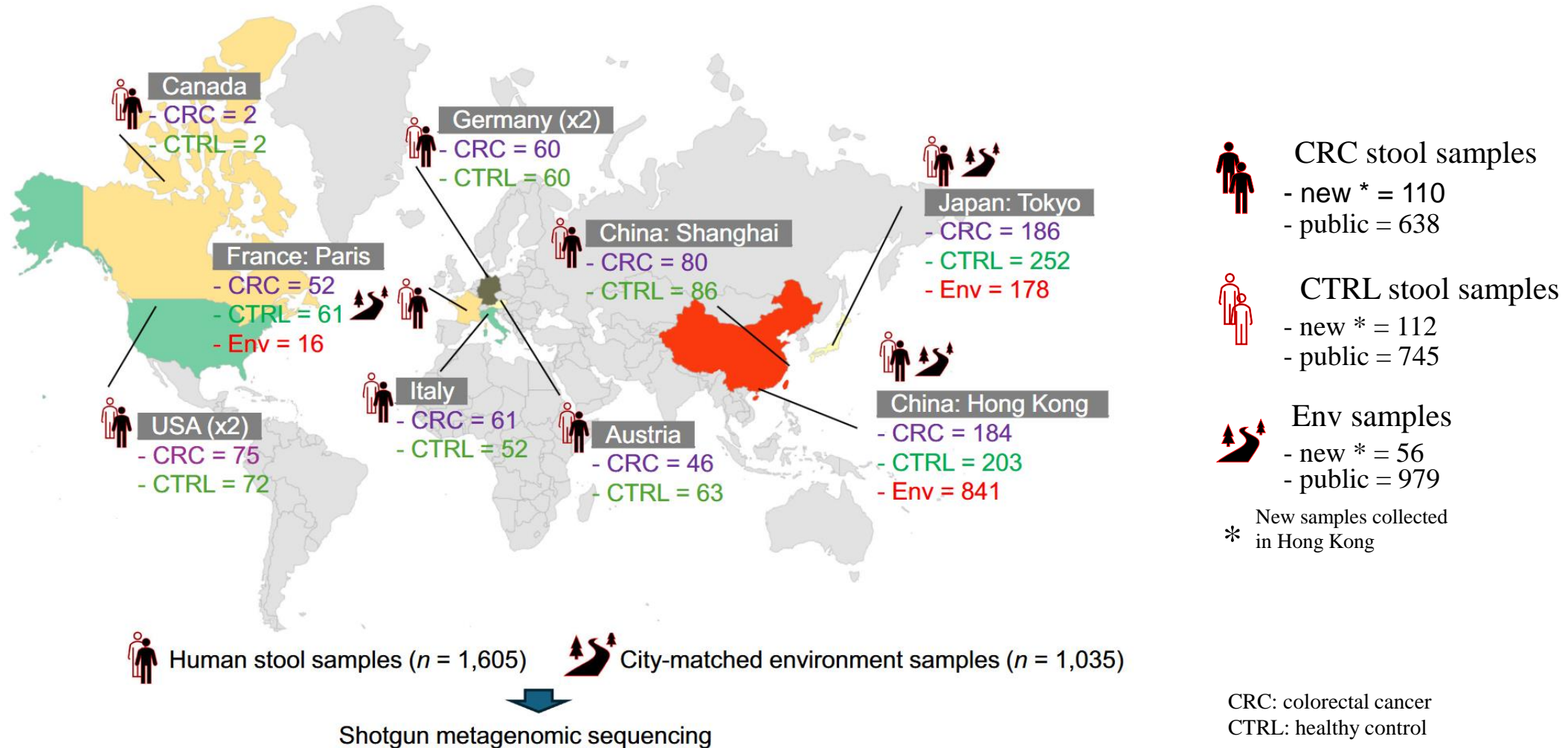


Figure 1 Study design. Human stool samples from colorectal cancer (CRC) patients and healthy subjects, and city-matched environment samples were collected worldwide.



Workflow

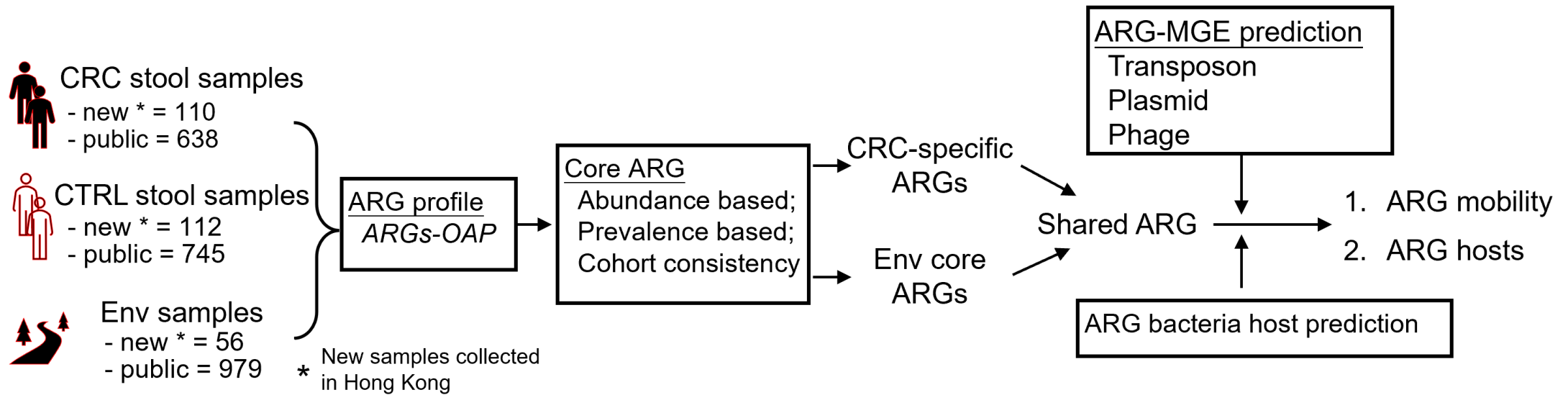


Figure 1 Analysis workflow. Summary of the workflow including analysis of core antimicrobial resistance gene (ARG) identification, ARG mobility, and ARG bacterial hosts.



ARG burden

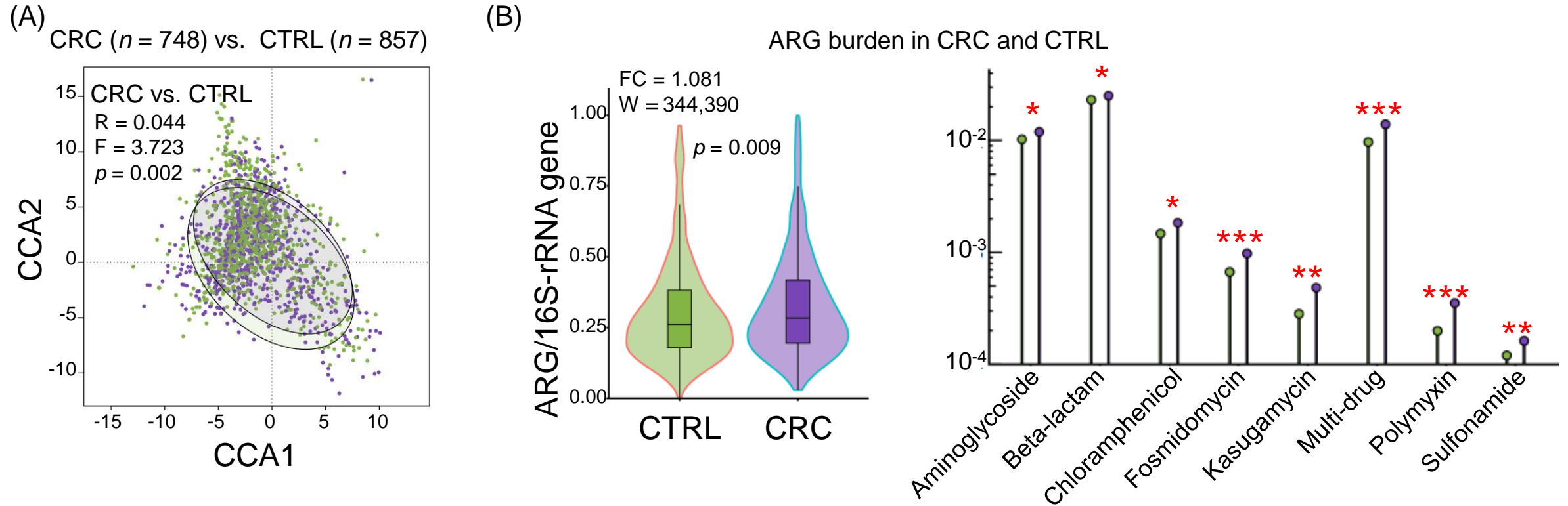


Figure 2. ARG profile in CRC patients and healthy individuals. (A) Overall ARG profile between CRC patients and CTRL. (B) Overall ARG burden (panel left) and resistant-specific ARG burden (panel right) between CRC patients and healthy subjects.



ARG similarity between the human and Env

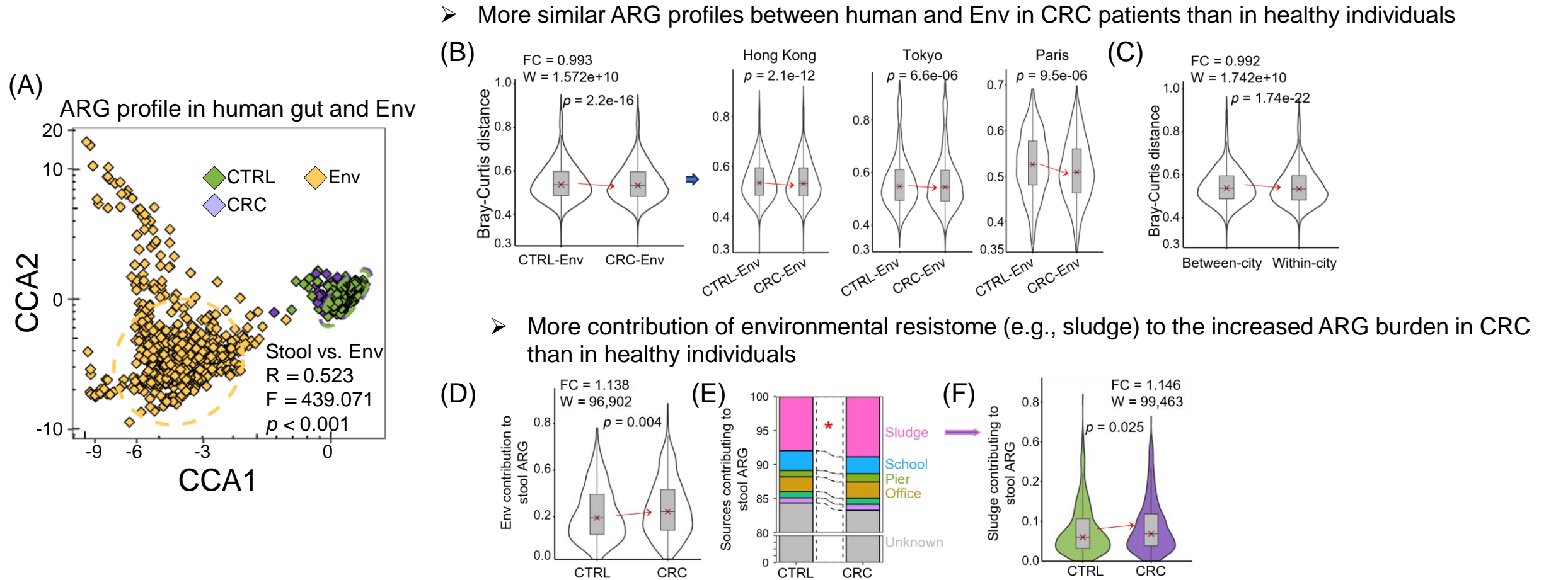


Figure 2 Connection of ARG profiles in human gut and environment. (A) ARG profiles between human gut and environmental samples. (B) Intra-city environment-gut ARG dissimilarity in CRC patients and CTRL. (C) Intra-city environment-gut ARG dissimilarity in CRC patients. (D-F) The impacts city-matched environmental ARGs on CRC patients



CRC-specific ARGs are shared with environmental core ARGs

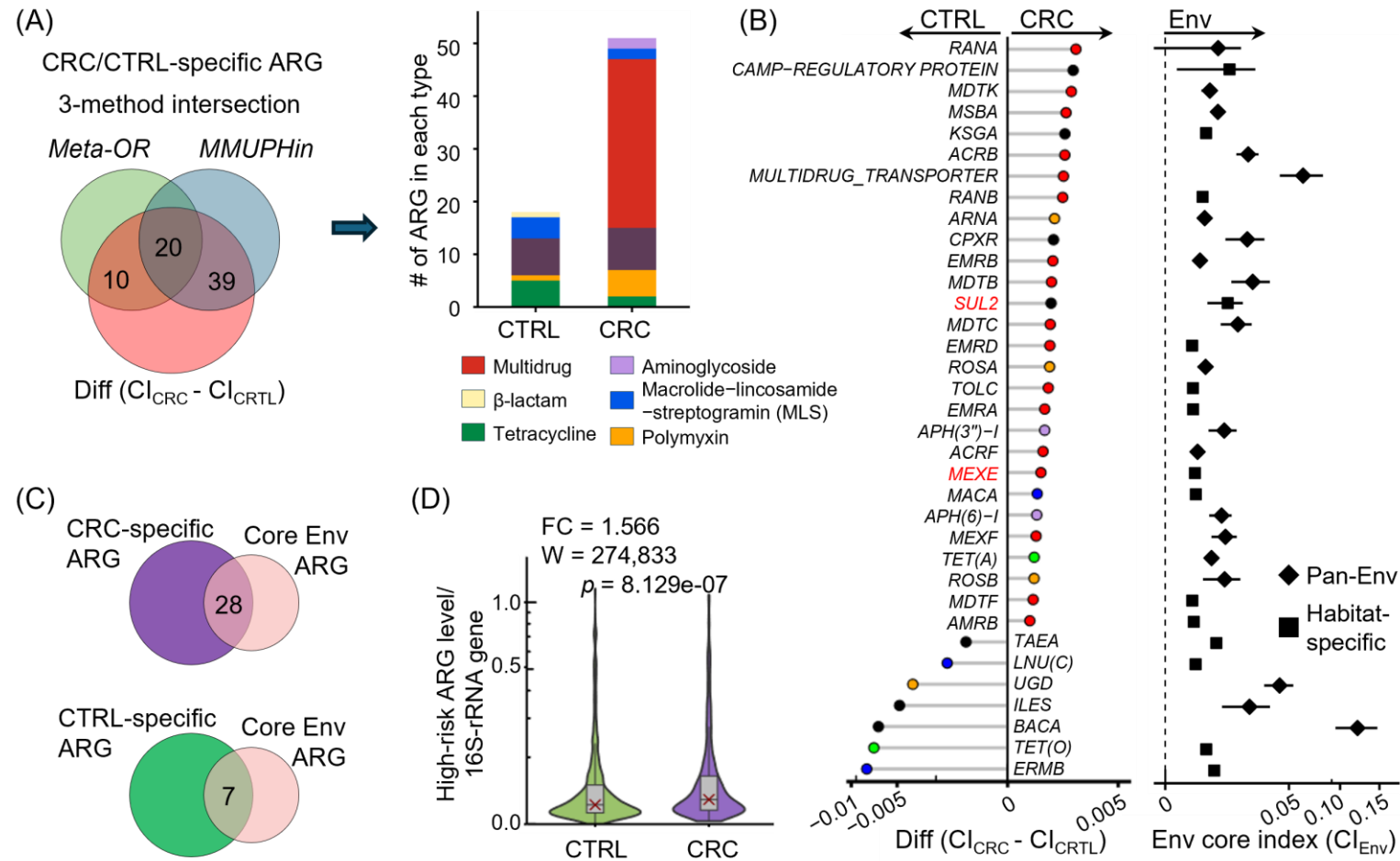


Figure 3 CRC-specific ARGs are shared with core environmental ARGs. (A) The differential ARGs between CRC patients and CTRL (B) CRC-/healthy-specific ARGs were shared with core environmental ARGs. (C) The amount of shared ARGs between CRC-/healthy-specific ARGs and core environment ARGs. (D) The level of high-risk ARGs.

More mobile ARGs and Higher ARG transmission efficiency in CRC

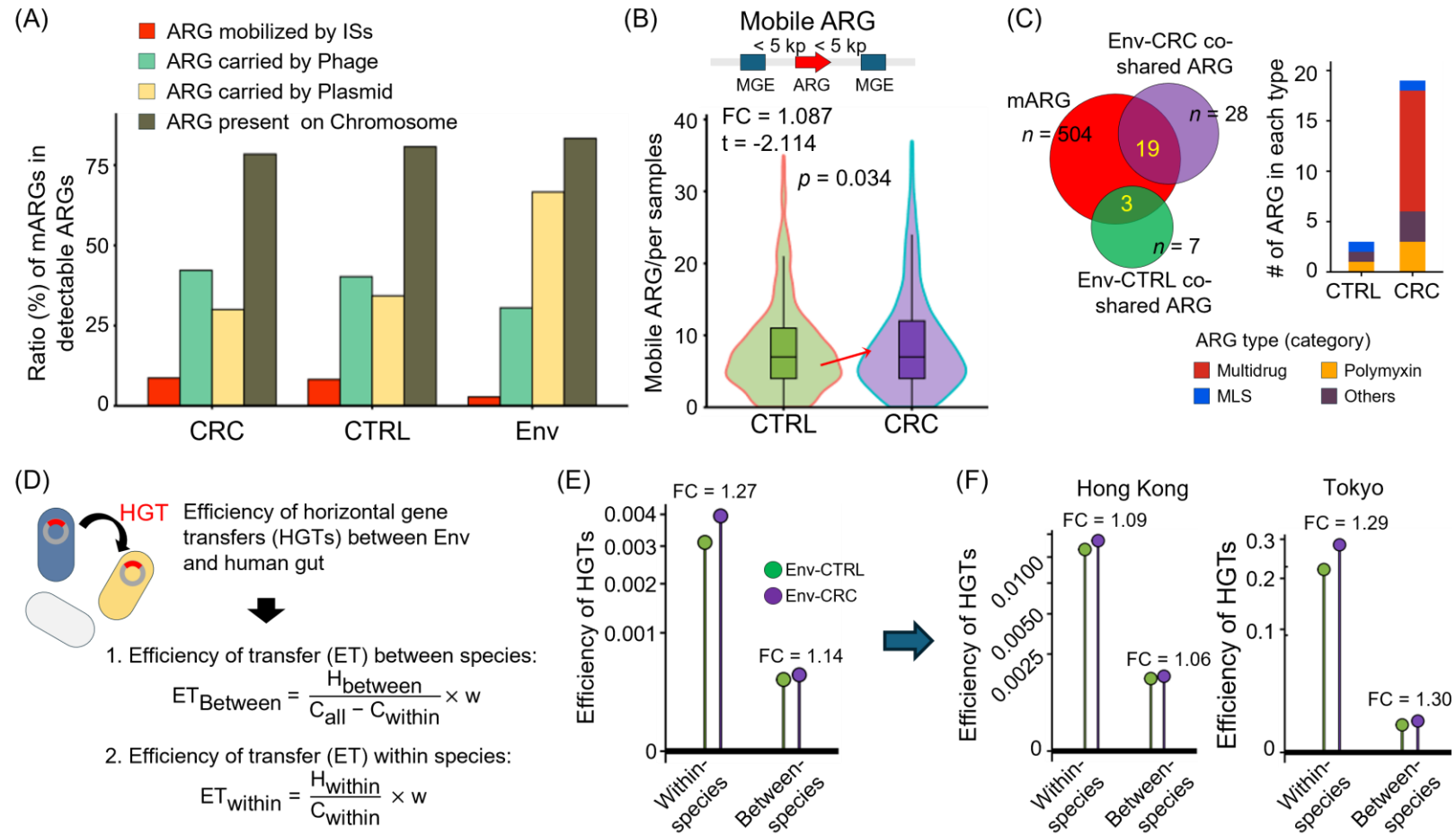


Figure 4 Mobile ARG (mARGs) in the human gut and environment. (A) The ratio of mARGs in each category (ISs, Phage, Plasmid, and Chromosome). (B) mARGs in CRC patients and CTRL. (C) The environment-gut co-shared mARGs in CRC patients and CTRL. (D-F) The environment-gut transmission efficiency in CRC and CTRL.

Hosts of mobile ARGs are opportunistic pathogenic bacteria

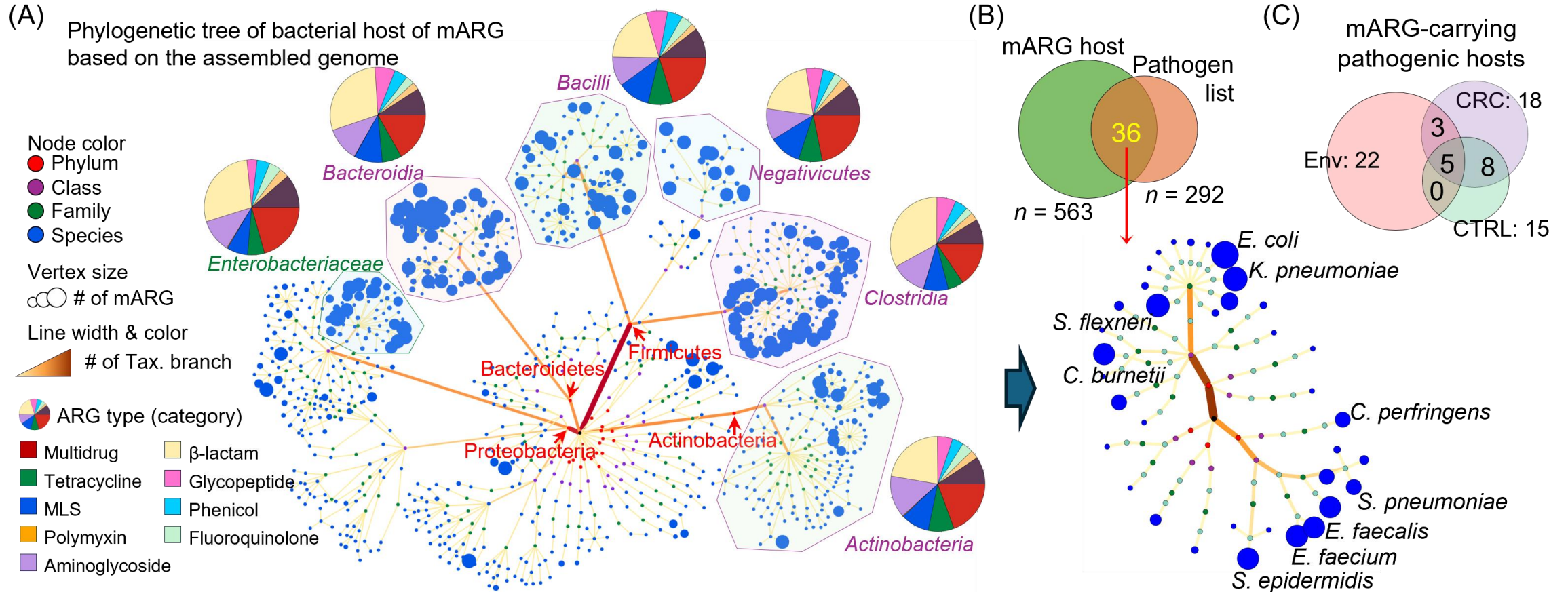


Figure 5 Bacterial hosts of mARGs. (A) Phylogenetic tree of bacterial hosts of mARG. (B) Number of mARG-carrying pathobionts. (C) More mARG-carrying pathobionts (environment-gut co-shared) were identified in CRC patients than in healthy subjects.

mARG-carrying pathobionts are enriched in CRC

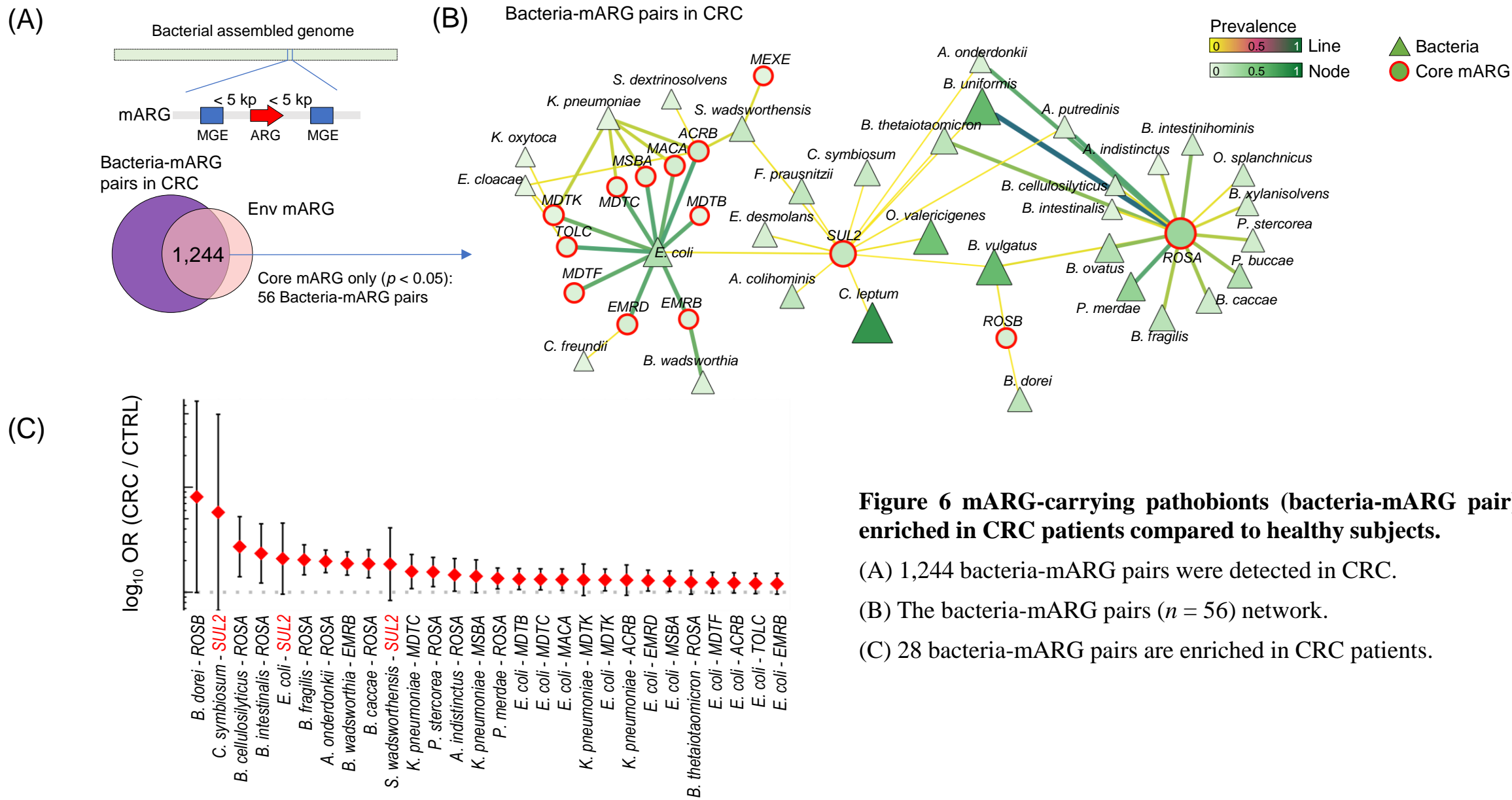


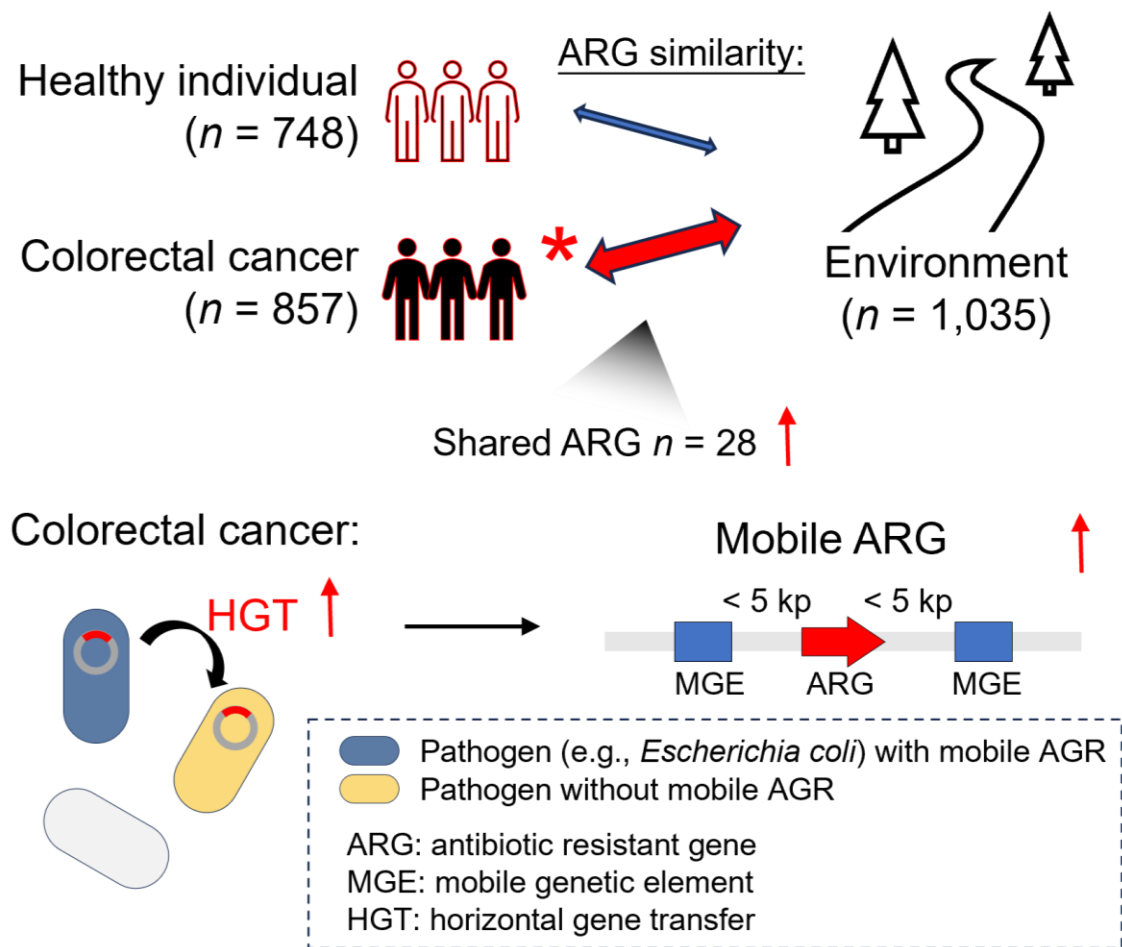
Figure 6 mARG-carrying pathobionts (bacteria-mARG pair) are enriched in CRC patients compared to healthy subjects.

(A) 1,244 bacteria-mARG pairs were detected in CRC.

(B) The bacteria-mARG pairs ($n = 56$) network.

(C) 28 bacteria-mARG pairs are enriched in CRC patients.

Summary

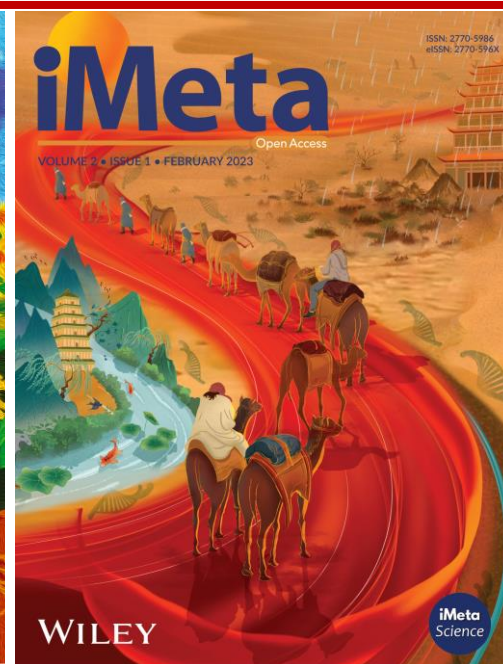


- Colorectal cancer (CRC) patients have a higher antimicrobial resistance gene (ARG) burden compared to healthy subjects.
- ARG profile between the city-matched environment and human gut is more similar in CRC patients than in healthy subjects.
- CRC patients had more environment-gut co-shared ARGs, more mobile ARGs (mARGs), and higher ARG transmission efficiency from the environment to gut, compared to healthy subjects.
- Bacterial hosts of mARGs were mainly pathogenic bacteria (e.g., *Escherichia coli* and *Clostridium symbiosum*), which were significantly enriched in CRC patients compared to healthy subjects.

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