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Genomic characterization and mapping of molecular factors driving the increased replication fitness of Arabian MERS-CoV lineage B5

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MERS-CoV is a highly pathogenic Betacoronavirus with a ~36% case-fatality rate and a zoonotic origin in dromedary camels. Clade B strains circulate in the Arabian Peninsula and are the primary cause of severe human infections, leading to sporadic outbreaks. In recent years, different clade B lineages have emerged, with lineage B5 replacing other clade B strains in the Middle East. Lineage B5 strains exhibit increased replicative fitness, higher resistance to type I interferons (IFNs), and reduced host immune activation, indicating enhanced viral fitness. Comparative genomic analyses with lineages B3, B4, and the EMC strain (clade A) reveal that B5 strains accumulate genetic changes, particularly in nsp3 and the Spike gene. To identify genetic determinants of B5 fitness, we used a reverse genetic system based on transformation-associated recombination (TAR) cloning. This system enables precise mapping of functional differences between recombinant MERS-CoVs. We generated 12 chimeric viruses by systematically exchanging genomic fragments between a lineage B5 strain and EMC. These were screened for replicative competence in Calu-3 cells, with or without type I IFN pre-treatment. Initial results suggest that genetic polymorphisms acquired in nsp3 and Spike could be responsible for the enhanced virulence of lineage B5 strains. Further assays are currently ongoing to depict specific virulence mechanisms and link them to fixed polymorphisms in B5 strains.

Keywords

MERS-CoV, TAR-cloning, emerging viruses

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Yes, I am a Junior Scientist.

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