Секция «Биоинформатика»

Microtubules are potential host targets to develop antiviral agents against the African swine fever virus

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African swine fever virus (ASFV) is the causal agent of a highly fatal disease of domestic swine and wild boar for which no effective vaccines and antiviral drugs are available. Recently, it has been shown that microtubule-targeting agents hamper the infection cycle of different viruses, raising the idea that microtubules can be potential host targets for antiviral drug development.[1][2] Is this study, we showed that well-known microtubule-targeting agents inhibited ASFV infection in Vero cells. Then, we conducted *in silico* screening against the colchicine binding site (CBS) of tubulin and found three new compounds with anti-ASFV activity. The most promising antiviral compound (6b) reduced ASFV replication in a dose-dependent manner ($IC_{50=}$19.5 μM) with no cellular ($CC_{50} > 500$ μM) and animal (white mice) toxicity (up to 100mg/kg). Results also revealed that compound 6b interfered with ASFV attachment, internalization and egress, with time-of-addition assays showing that compound 6b has higher antiviral effects when added within 2 to 8 hours post-infection. This compound significantly inhibited the viral DNA replication and disrupts the viral protein synthesis. Experiments with ASFV-infected porcine macrophages disclosed that antiviral effects of the compound 6b were similar to its effects in Vero cells. Tubulin polymerization assay and confocal microscopy demonstrated that compound 6b promoted tubulin polymerization, acting as a microtubule-stabilizing rather than destabilizing agent in cells. The 4D molecular docking studies demonstrated that compound 6b could interact with the taxol binding site. In conclusion, this work emphasizes the idea that microtubules have essential role during ASFV replication cycle and can be targets for drug development against ASFV.[3]

References

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