



Opisthorchis felineus extracellular vesicles increase cell proliferation and migration rates of human H69 cholangiocytes

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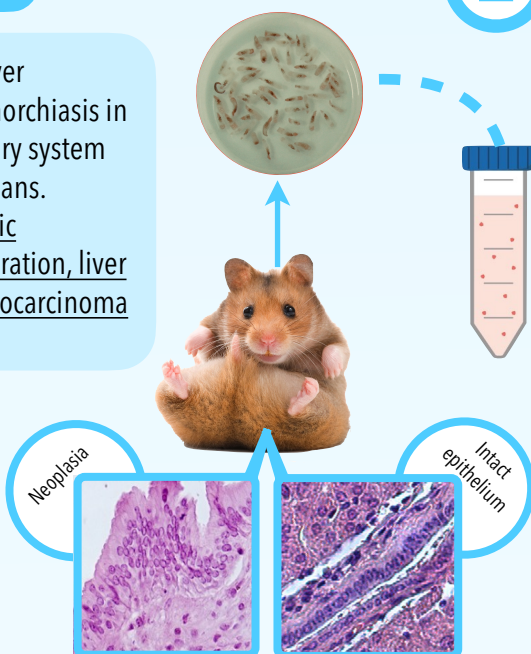
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1 Introducing

Opisthorchis felineus, is a food-borne liver trematode and the main cause of opisthorchiasis in Russia and Europe. It affects hepatobiliary system of fish-eating mammals, including humans. Opisthorchiasis is associated with chronic inflammation, biliary epithelium proliferation, liver fibrosis, and even might cause cholangiocarcinoma among chronically infected individuals.

Secreted proteins and extracellular vesicles of liver flukes might play an important role in the development of pathology.

The aim was to investigate the influence of adult worms and their extracellular vesicles on cell proliferation and migration rates of human H69 cholangiocytes.



2 Materials and methods

Adult *Opisthorchis felineus* liver flukes were extracted from laboratory hamsters previously infected with the metacercariae. Adult flukes were cultured in the media.

EVs were extracted from the cultivation media and purified, using ultrafiltration approach.

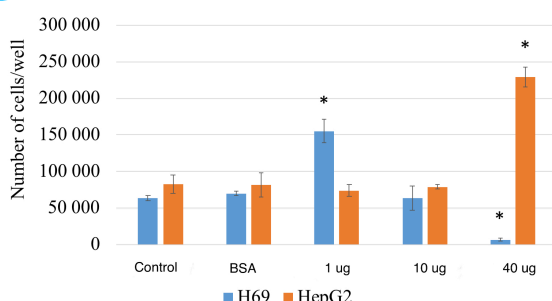
EVs were co-cultured with H69 or HepG2 cells.

1-6 flukes were co-cultured with H69 or HepG2 cells using a non-contact approach with Transwell plates inserts.

Cell migration analysis was performed after 14 days of co-cultivation with EVs using traditional scratch test.

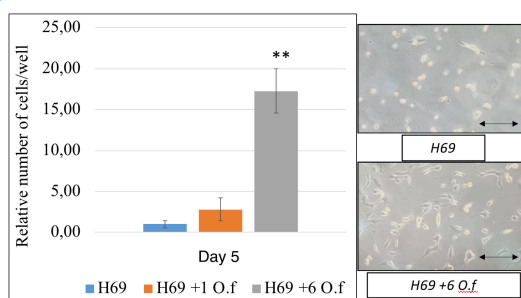
3 Results

Influence of EVs on proliferation



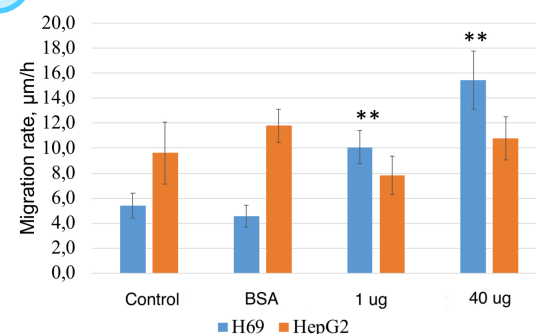
Proliferation of human cholangiocytes H69 was 2 times increased after cultivation with the EVs, but with increasing EVs concentration the number of cells was reduced.

Influence of flukes on proliferation



Proliferation of human cholangiocytes H69 was 4-17 times increased after co-cultivation with the liver flukes and was accompanied by cell morphological changes.

Influence on cell migration



The rate of H69 cell migration, (not HepG2) was increased 2 times after 1 µg EVs, and was increased 3 times after 40 µg EVs.

4 Conclusion

Specific mitogenic effect of liver fluke extracellular vesicles on proliferation and migration of human cholangiocytes *in vitro* may reflect the mechanisms of development of precancerous biliary intraepithelial neoplasia during opisthorchiasis *in vivo*.

References

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