PD42-11

Cigarette Smoke, E-cigarettes and Bladder Cancer Cell-Derived Extracellular Vesicles induce Bladder Carcinogenesis

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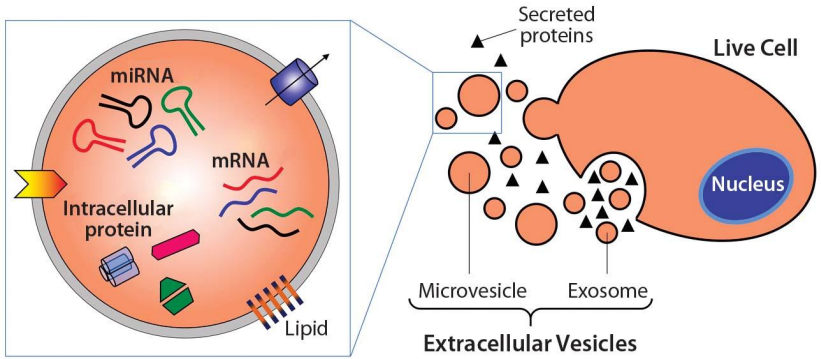
Cancer-derived extracellular vesicles



(Smith *et al.* 2015)

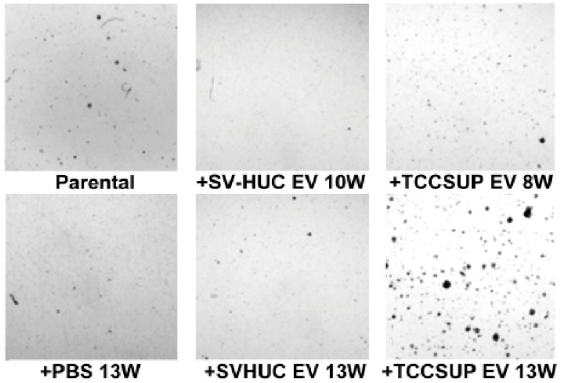
Extracellular vesicles (EVs):

- Contain bioactive molecules from the donor cells.
- Affect recipient cells by internalization or surface interactions.
- Reported to advance all cancer hallmarks and promote carcinogenesis. (Kanada *et al.* 2016)
- Cigarette smoke-induced release of EVs is associated with development of lung disease, lung cancer and oral cancer. (Ryu *et al.* 2018)

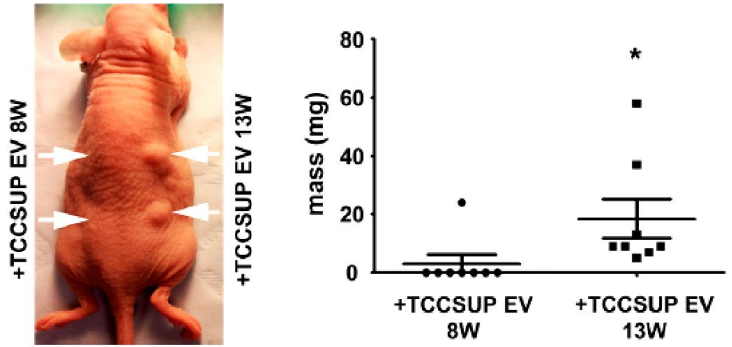
Long-term cancer EV treatment increases maglignant transformation frequency in urothelial cells

SV-HUC: immortalized normal urothelial cell line
TCCSUP: Grade 4 transitional cell carcinoma cell line

Colony formation in soft agar



Tumorigenesis in nude mouse xenografts



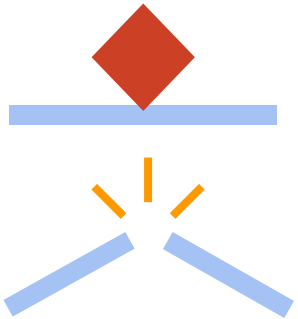
(Wu *et al.* 2018)

Carcinogensis by cigarette smoke

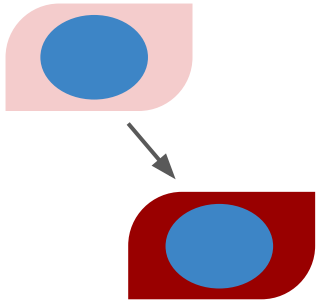
Contains more than 60 carcinogens including specific nitrosamines and aromatic amines.

50%

50% of bladder cancer cases are related to cigarette smoke.



Causes DNA adducts which result in DNA damage and eventually cancer.



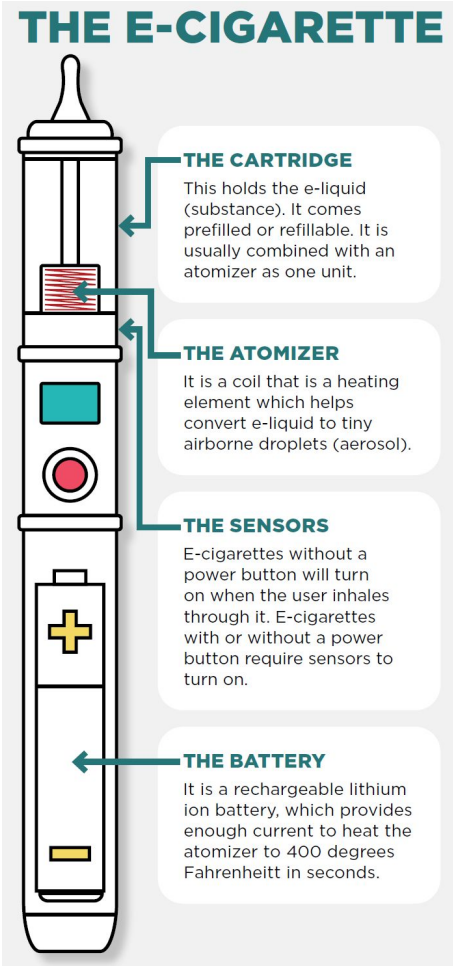
Associated with adverse bladder cancer progression, poor chemotherapy response, and recurrence.

E-cigarettes

- How they work:

Users inhale to activates device → coil heats up to 1000℃ (Chen *et al.* 2018) → aerosolizes e-liquid in the cartridge → E-liquid consumed by users

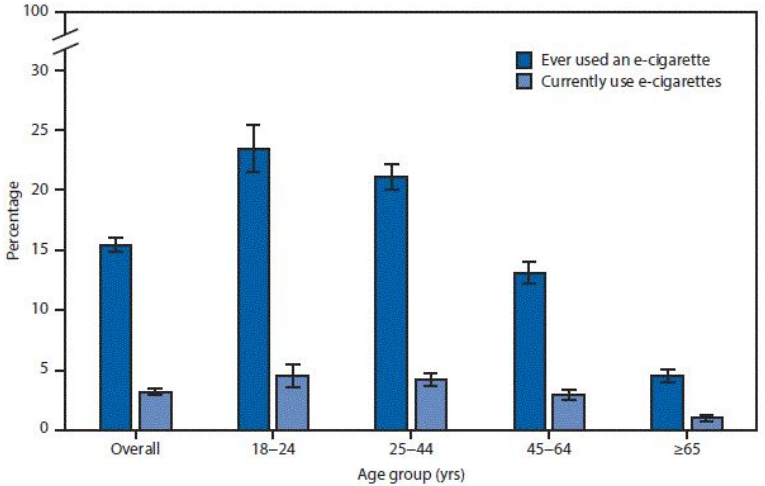
- Content of e-liquid:
  - Solvent – propylene glycol (PG), vegetable glycerin (VG)
  - Nicotine
  - Flavor

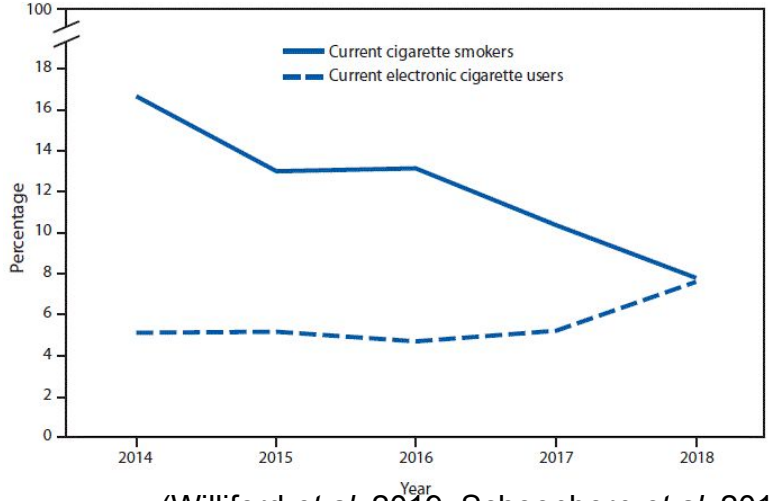


(CDC.gov)

E-cigarettes

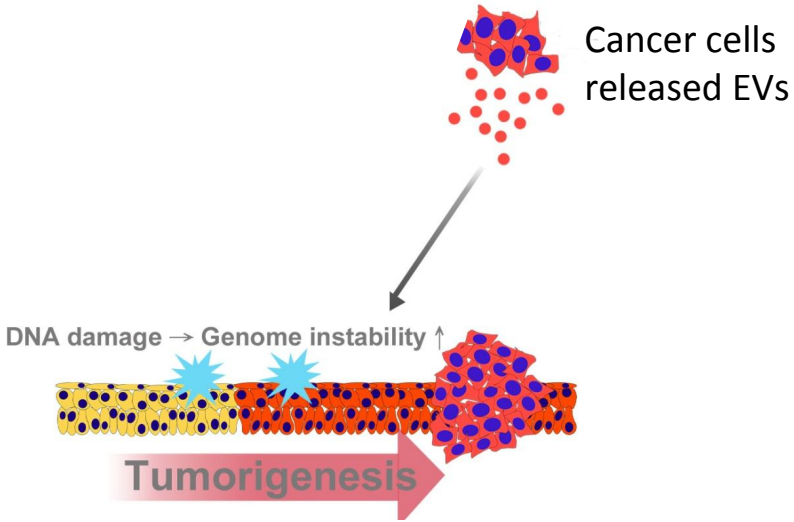
- Popularity in adults over 18 years (2016):
  - Ever used e-cigarettes: 15.4%
  - Currently use e-cigarettes: 3.2%
- Popularity among age 18-24 adults is increasing as cigarette use declines.
- Have potential as a substitute for cigarettes among current smokers.
- Assessment of long-term health effects is still required



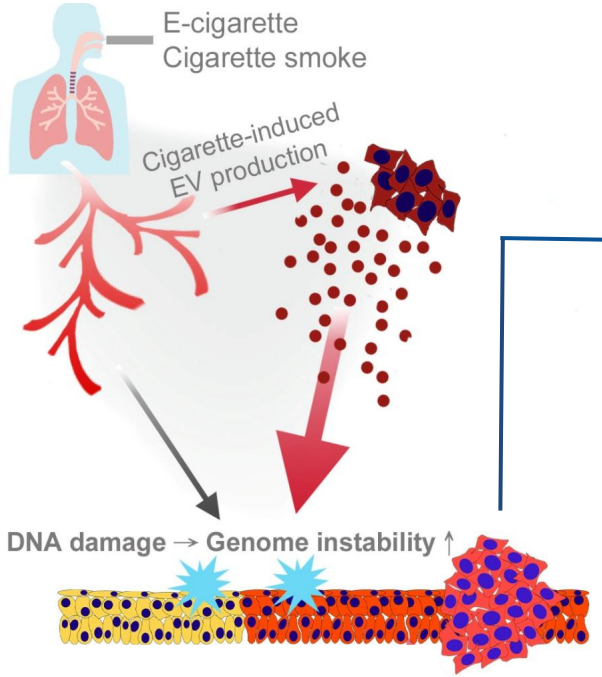


(Williford *et al*, 2019; Schoenborn *et al*, 2017)

Hypothesis


Cancer cells
released EVs
DNA damage → Genome instability ↑
Tumorigenesis

Hypothesis

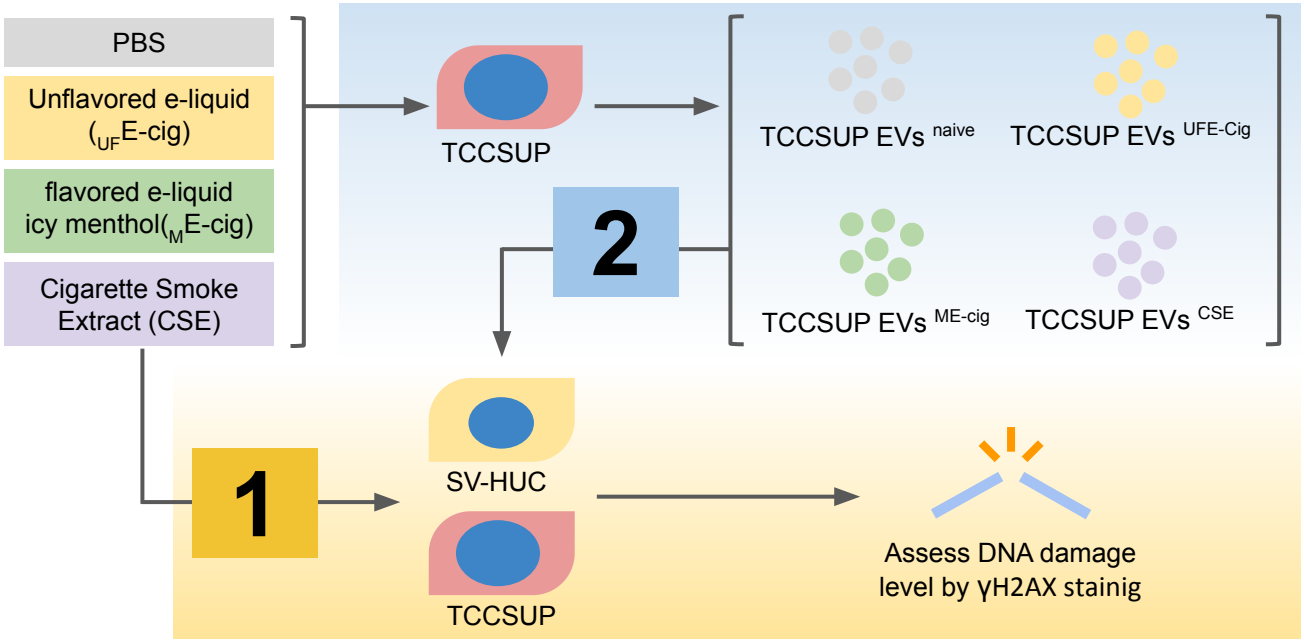


- **Tumorigenesis (recurrence)**
- **Poor chemotherapy response**
- **Disease Progression**

Experimental design

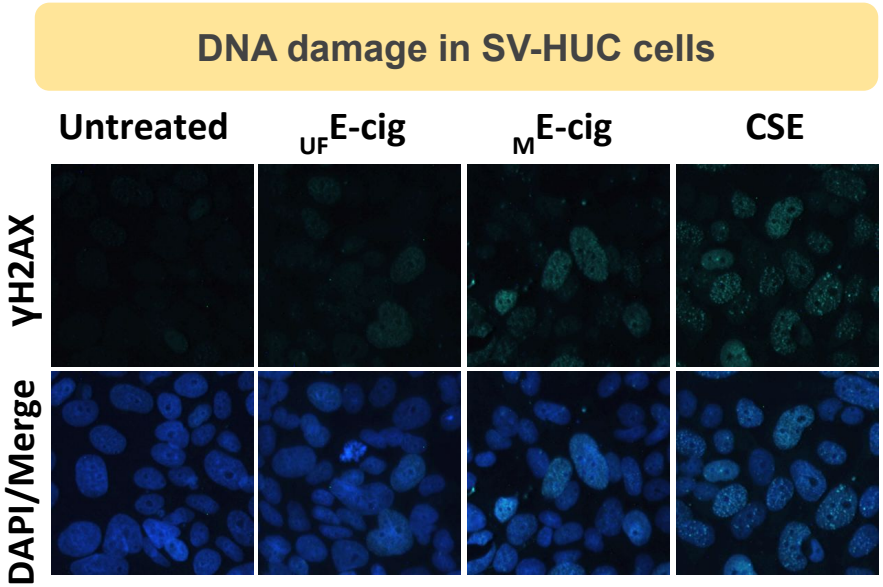
SV-HUC: immortalized normal urothelial cell line

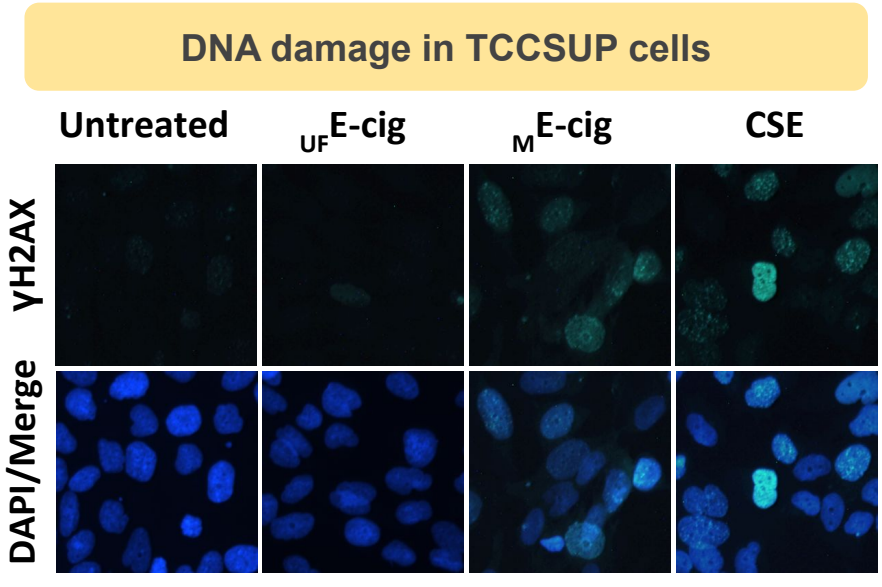
TCCSUP: Grade 4 transitional cell carcinoma cell line



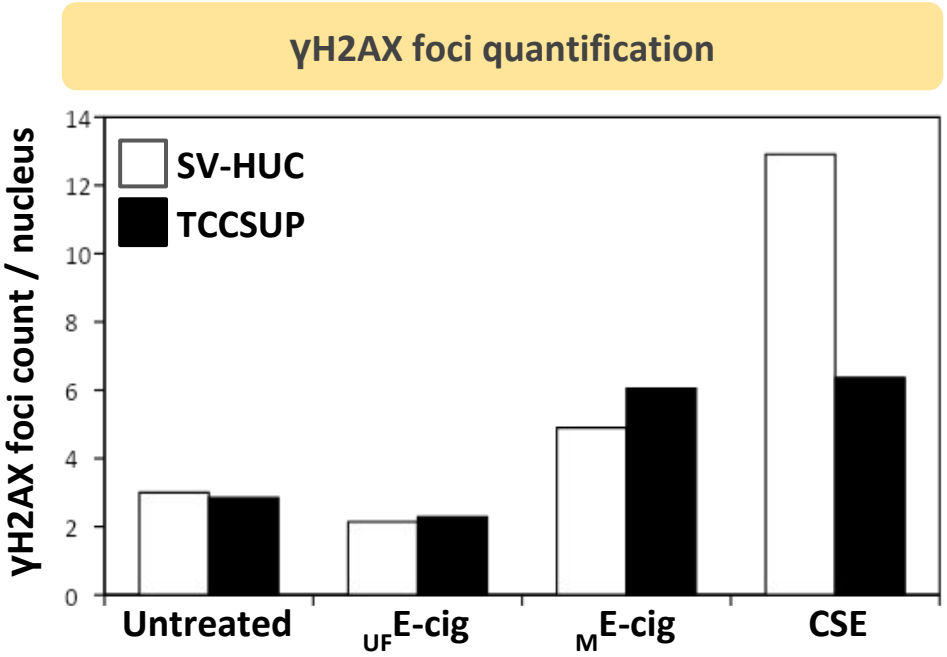
1. To assess the direct carcinogenic impact of cigarette smoke and e-liquids on treated cells.
2. To assess the carcinogenicity of EVs derived from cancer cells exposed to cigarette smoke or e-liquids

CSE and e-liquid are genotoxic to both cancer and normal cells



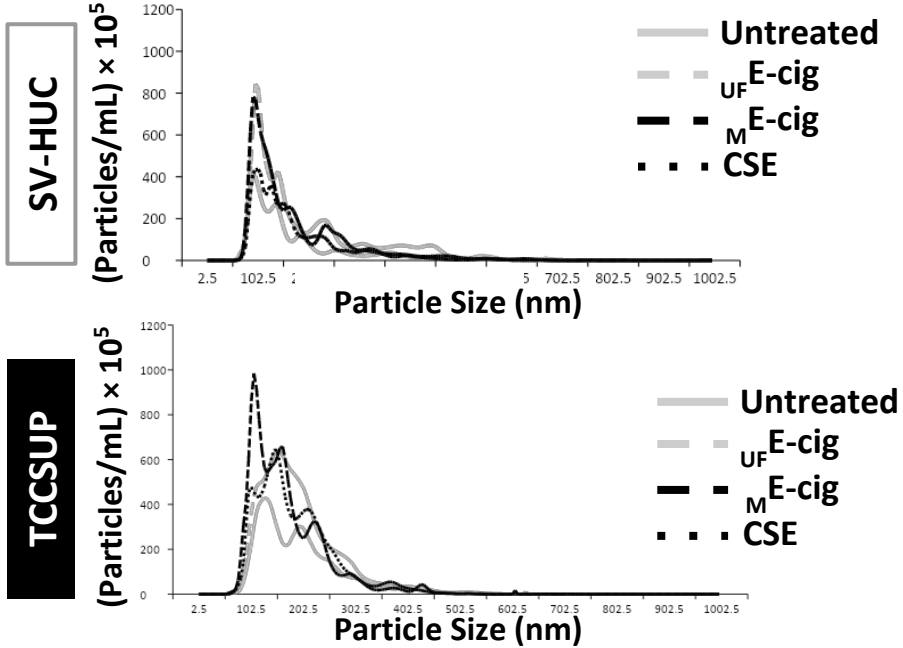


CSE and mentholated e-liquid are genotoxic to both cancer and normal cells

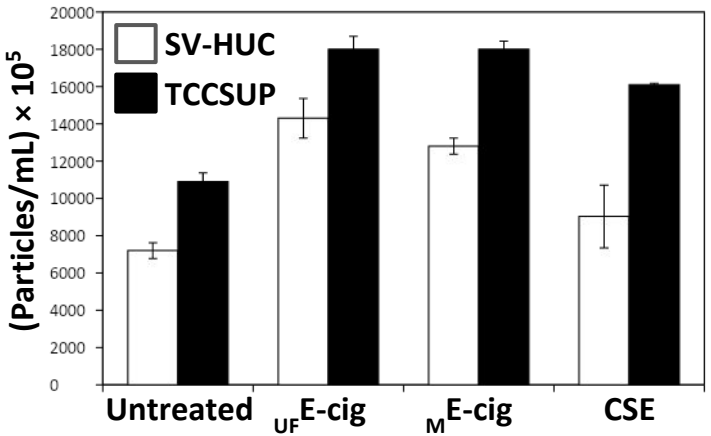


CSE and e-liquid up-regulate TCCSUP and SV-HUC EV production

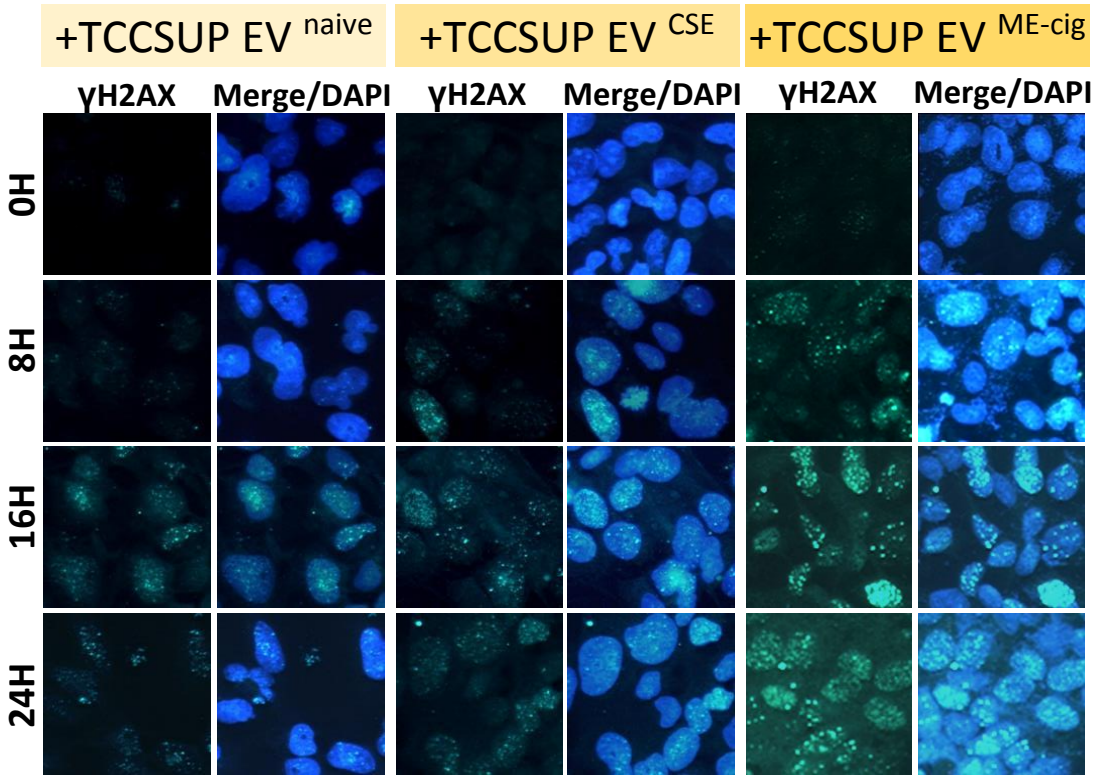
EV size distribution



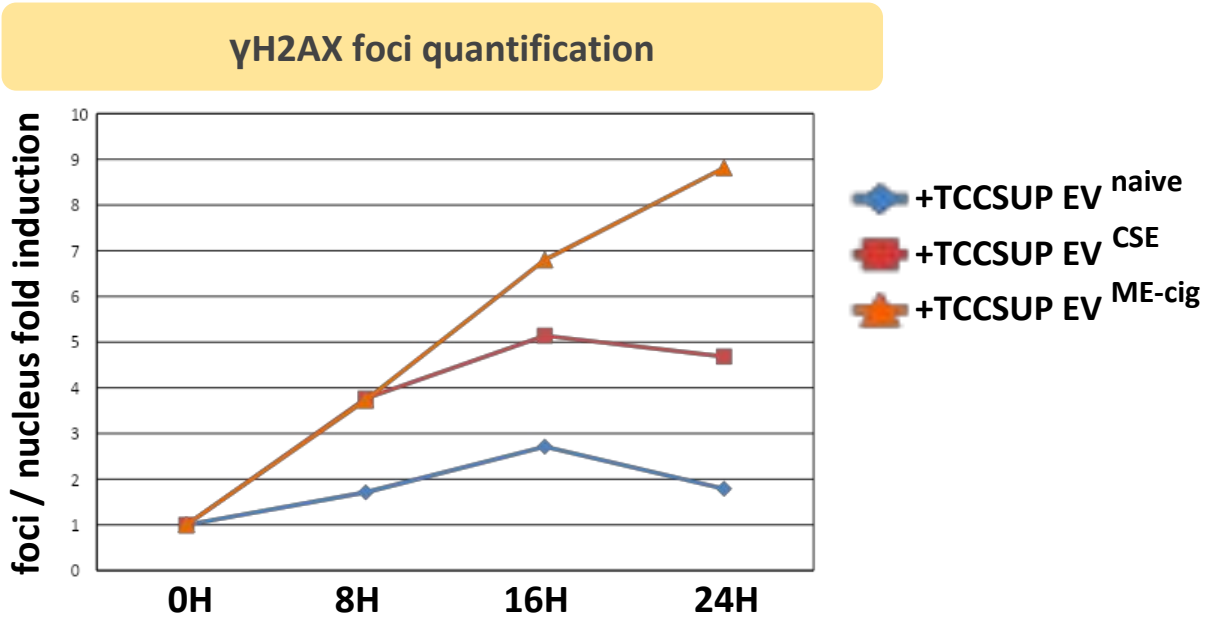
EV production



EVs collected from treated cancer cells are more genotoxic than naïve cancer EVs

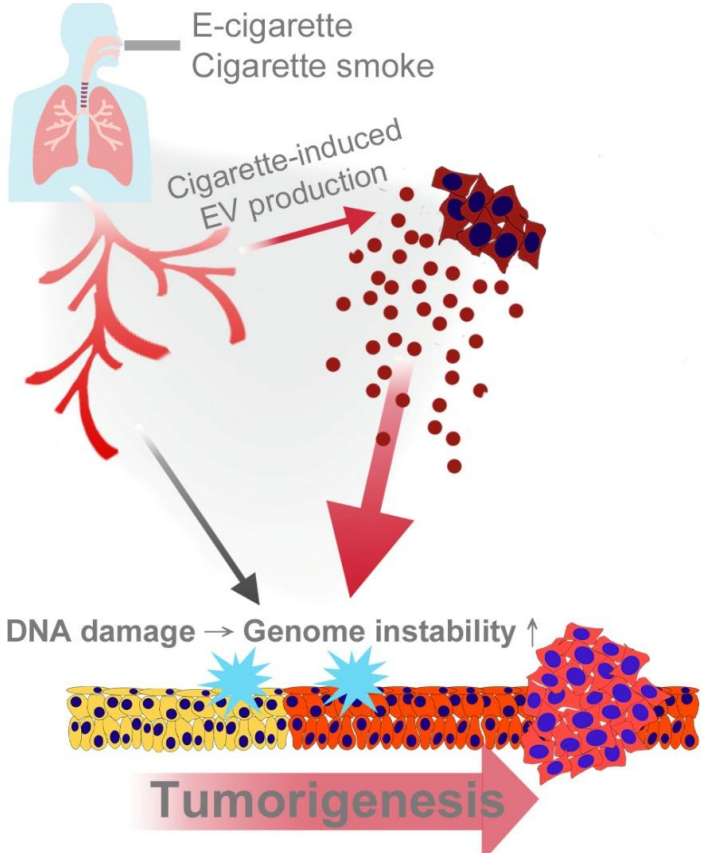


EVs derived from flavored e-liquid-treated cancer cells induce more severe DNA damage



Summary

- CSE and flavored e-liquid are directly genotoxic to both cancer and normal cells.
- unflavored e-liquid does not cause DNA damage in treated cell lines.
- CSE and flavored e-liquid treatment increases EV production in both cancer and normal cells
- EVs from treated cancer cells have an increased ability to create further DNA damage in recipients.



Questions?

Please contact us by email

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