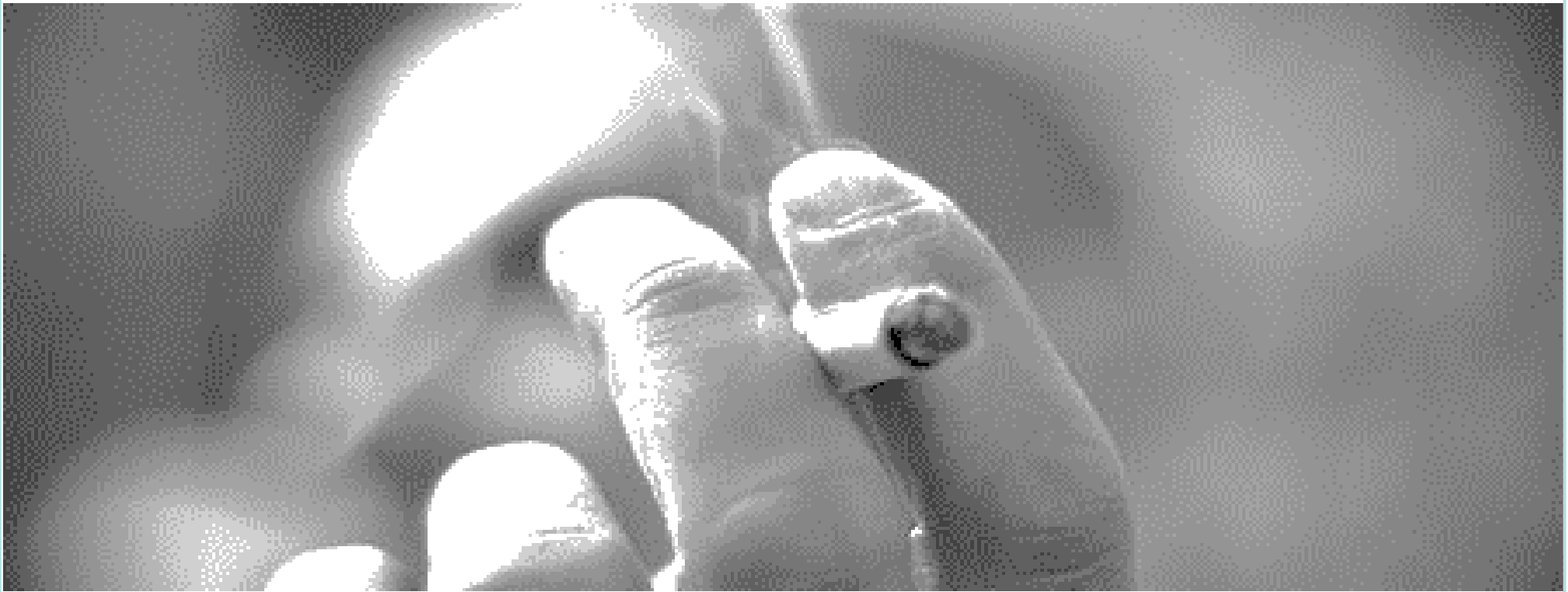
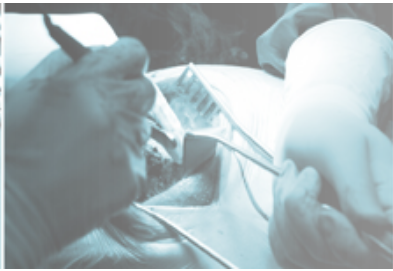
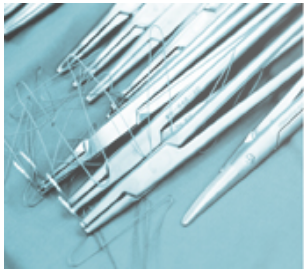


Nicotine Promotes Tumor Growth and Metastasis in Mouse Models of Lung Cancer

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Background

Smoke ingredients

Acetone – found in nail polish remover

Acetic Acid – an ingredient in hair dye

Ammonia – a common household cleaner

Arsenic – used in rat poison

Benzene – found in rubber cement

Butane – used in lighter fluid

Cadmium – active component in battery acid

Carbon Monoxide – released in car exhaust fumes

Formaldehyde – embalming fluid

Hexamine – found in barbecue lighter fluid

Lead – used in batteries

Naphthalene – an ingredient in moth balls

Methanol – a main component in rocket fuel

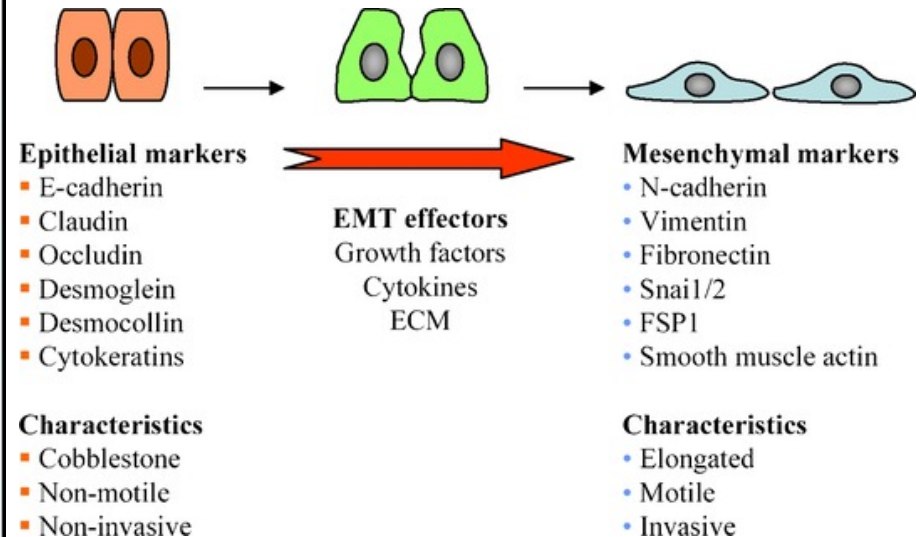
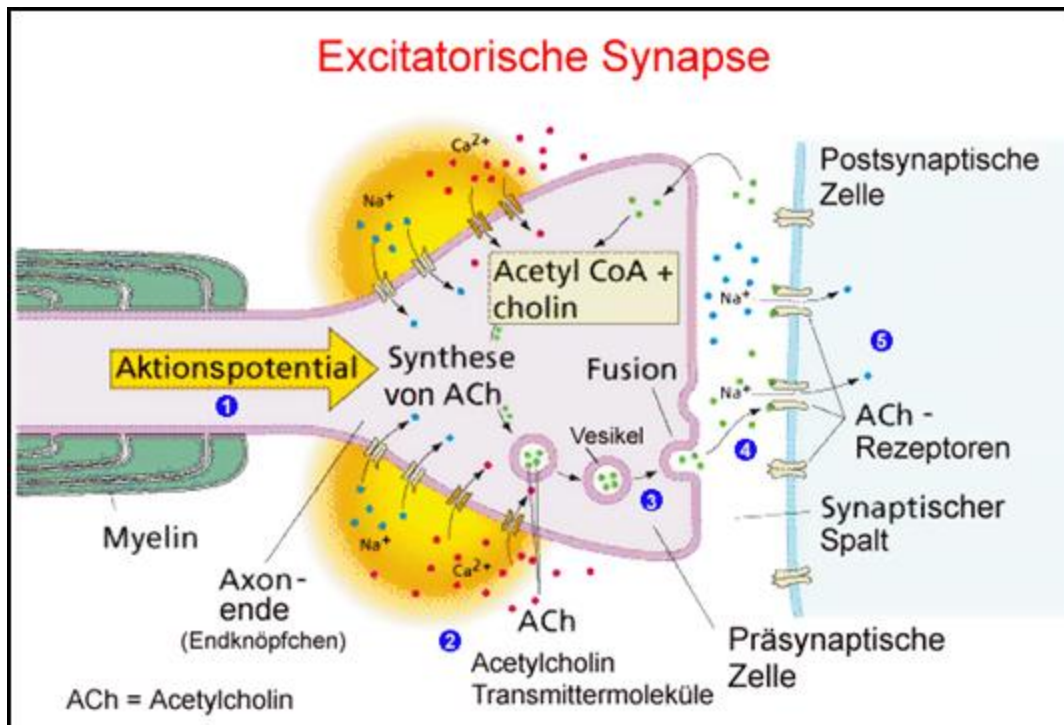
Nicotine – used as insecticide

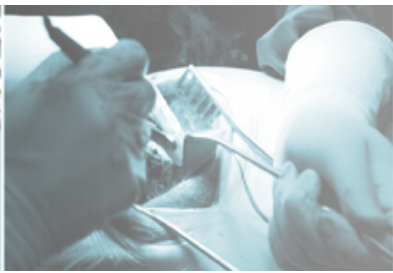
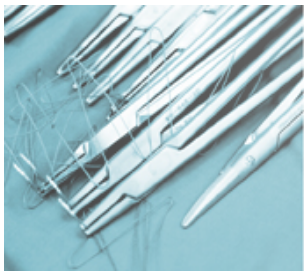
Tar – material for paving roads

Toluene - used to manufacture paint

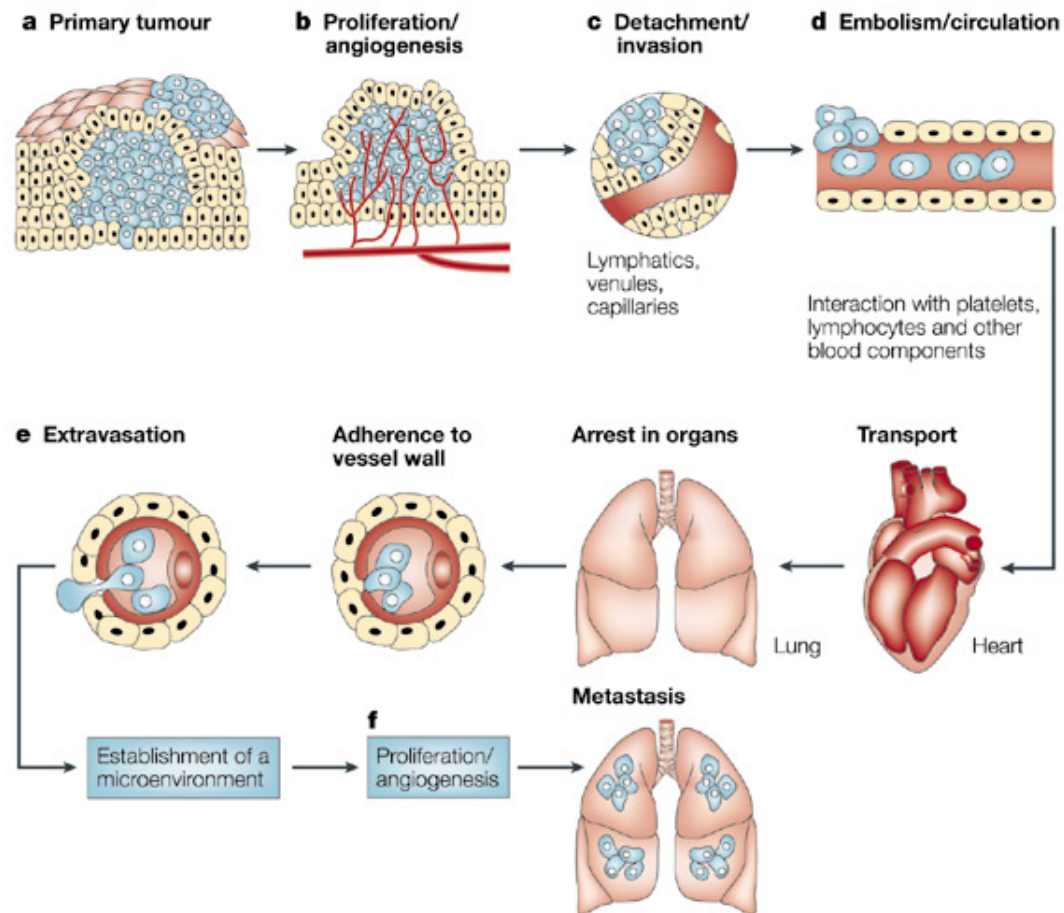


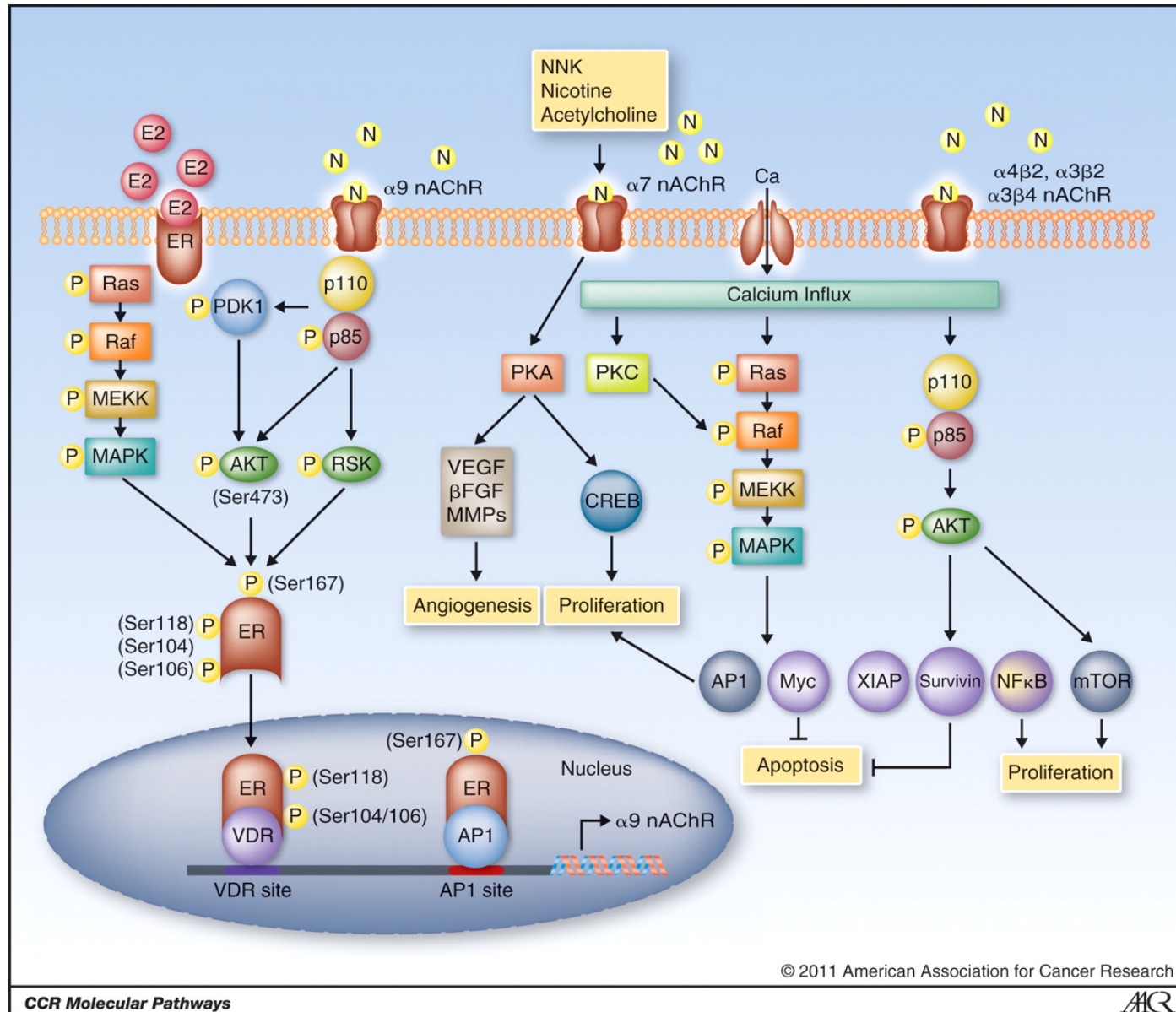
Background

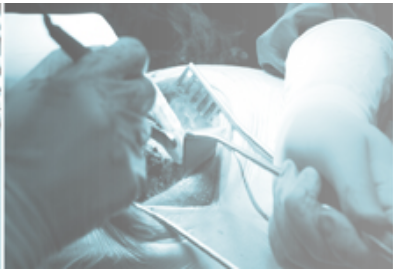
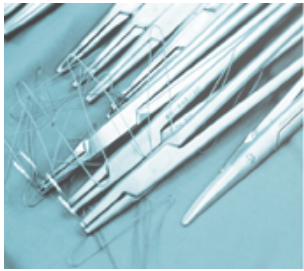




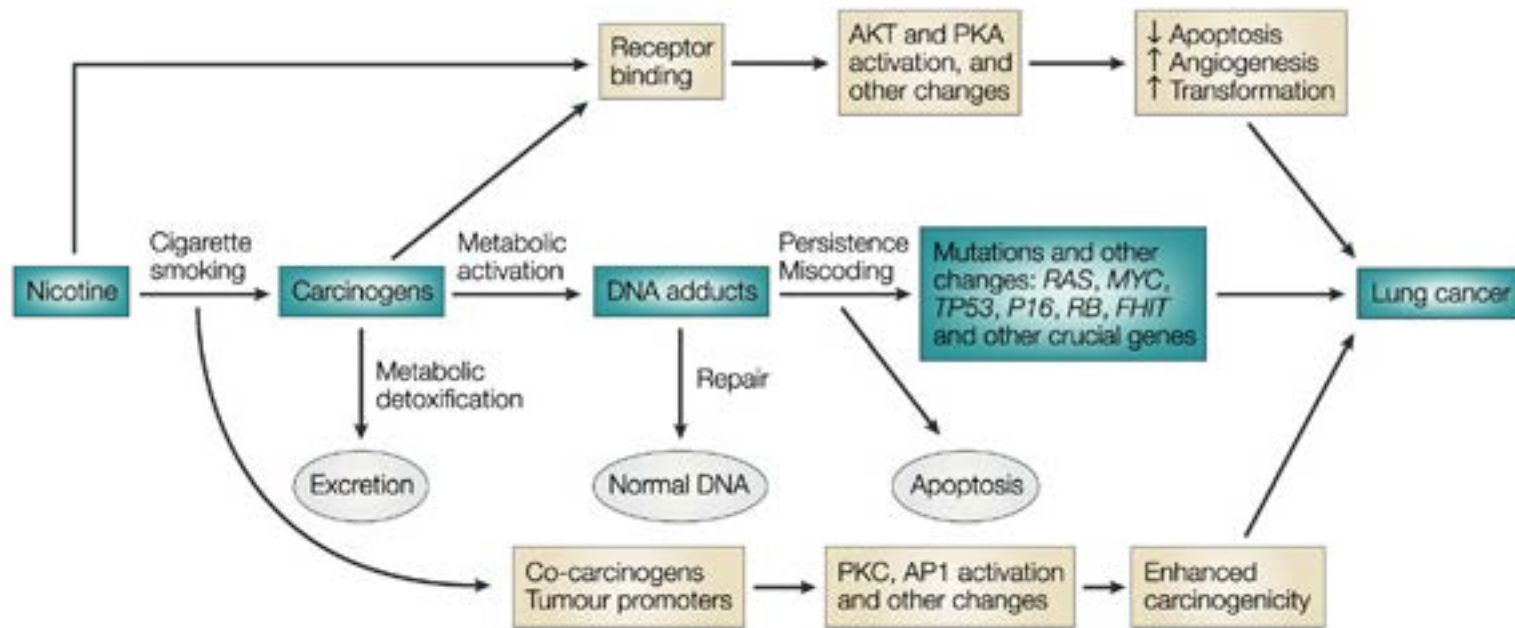
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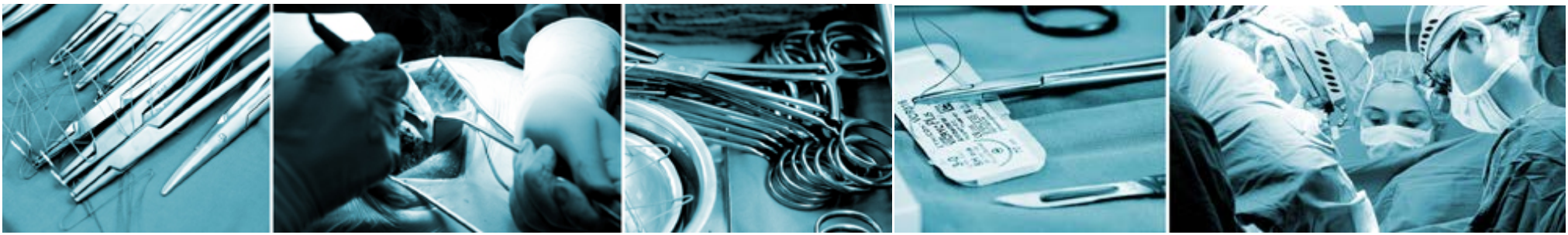






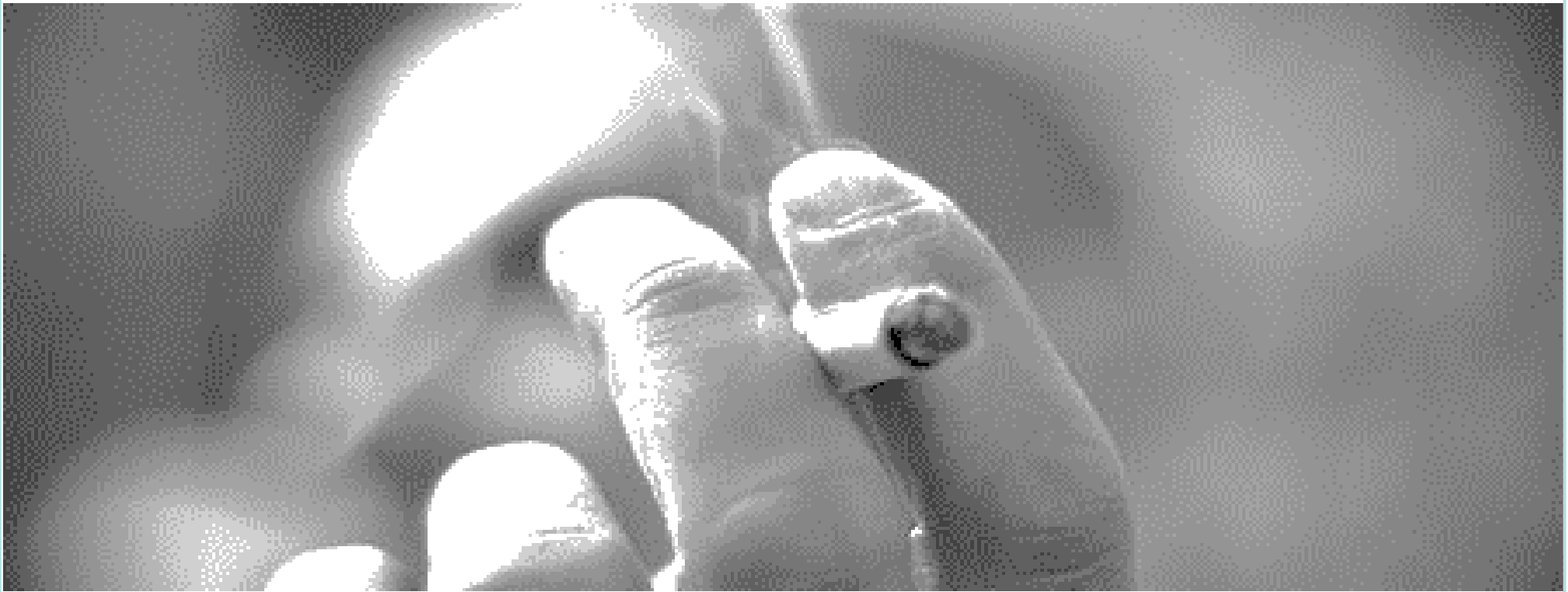
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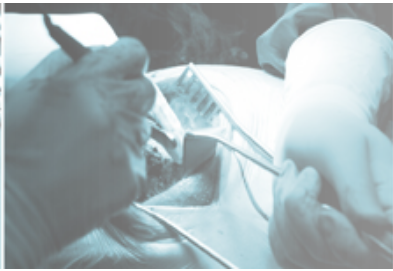
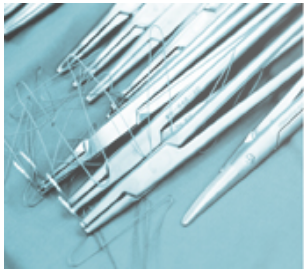




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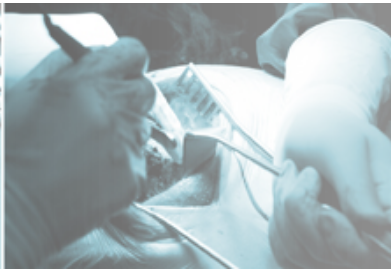
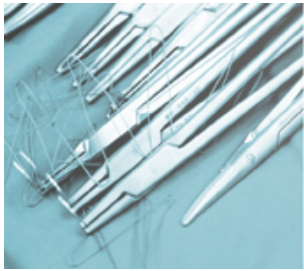
Methods

in vitro assays

- Bromodeoxyuridine assay
- RT-PCR
 - alpha7-nAChR
- ELISA
 - Cotinine levels
 - Noradrenaline
 - Adrenaline
- Immunohistochemistry
 - alpha7-nAChR
 - E-Cadherin
 - beta-Catenin
 - ZO-1 (*zonula occludens*)

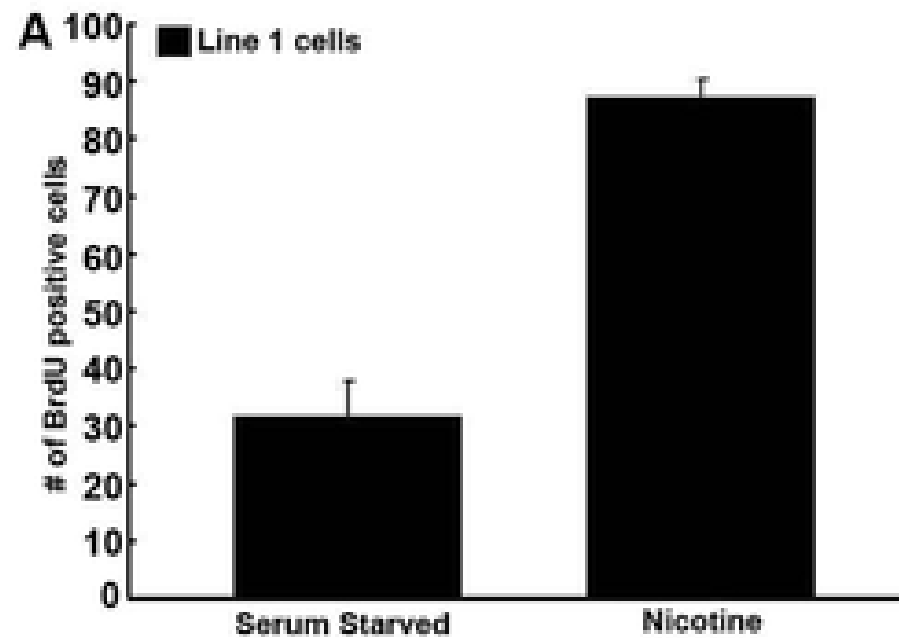
cell culture
cell lysate

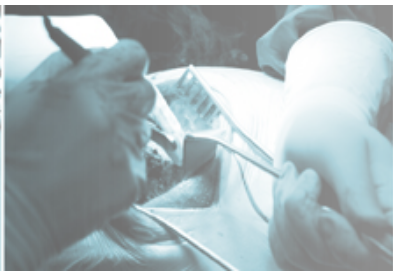
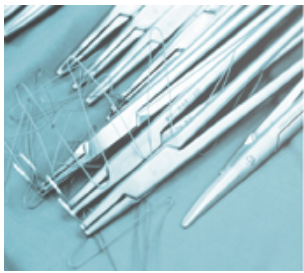
urine
cell supernatants (not shown)
cell supernatants (not shown)
excised tumors



Results

Figure 1A. Nicotine promotes the growth of Line1 cells.

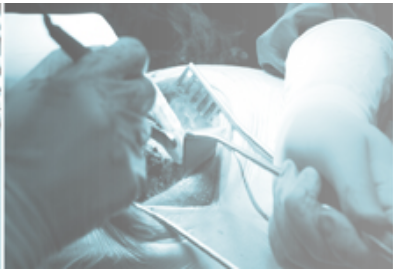
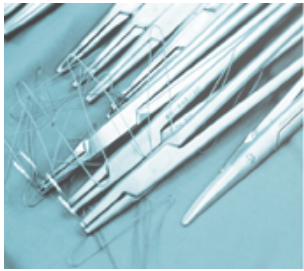




Methods

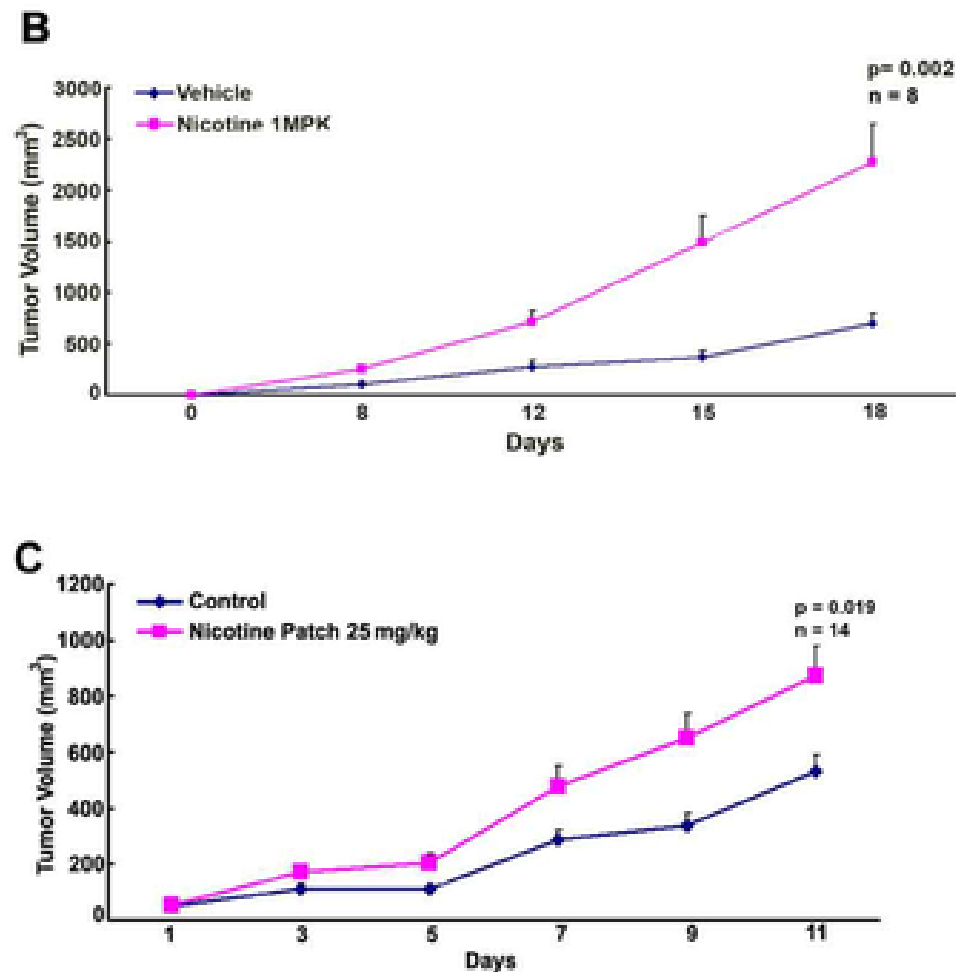
BALB/c tumor growth & metastasis *in vivo*

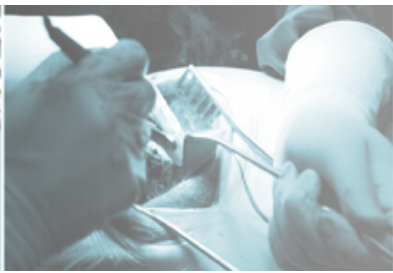
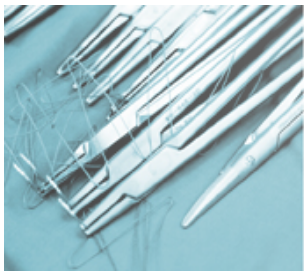




Results

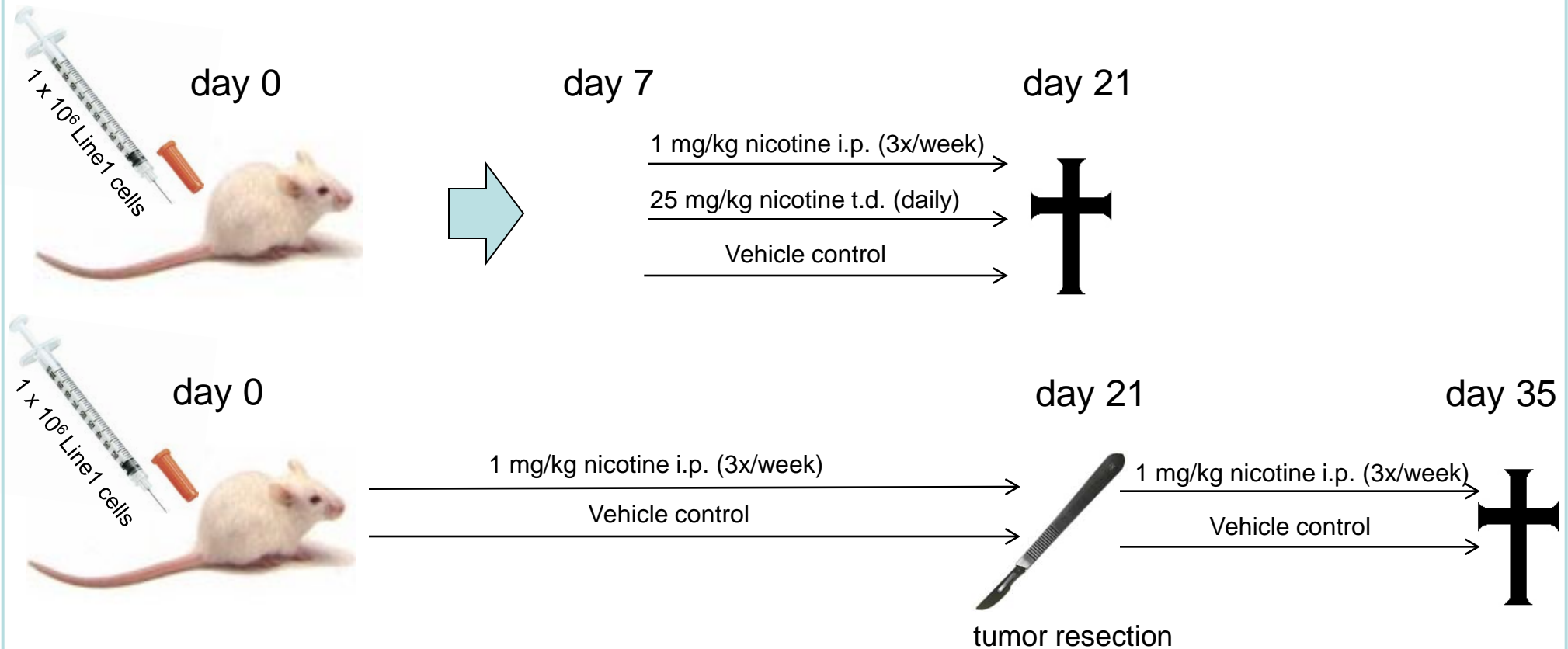
Figure 1BC. Nicotine promotes the growth *in vivo*.





Methods

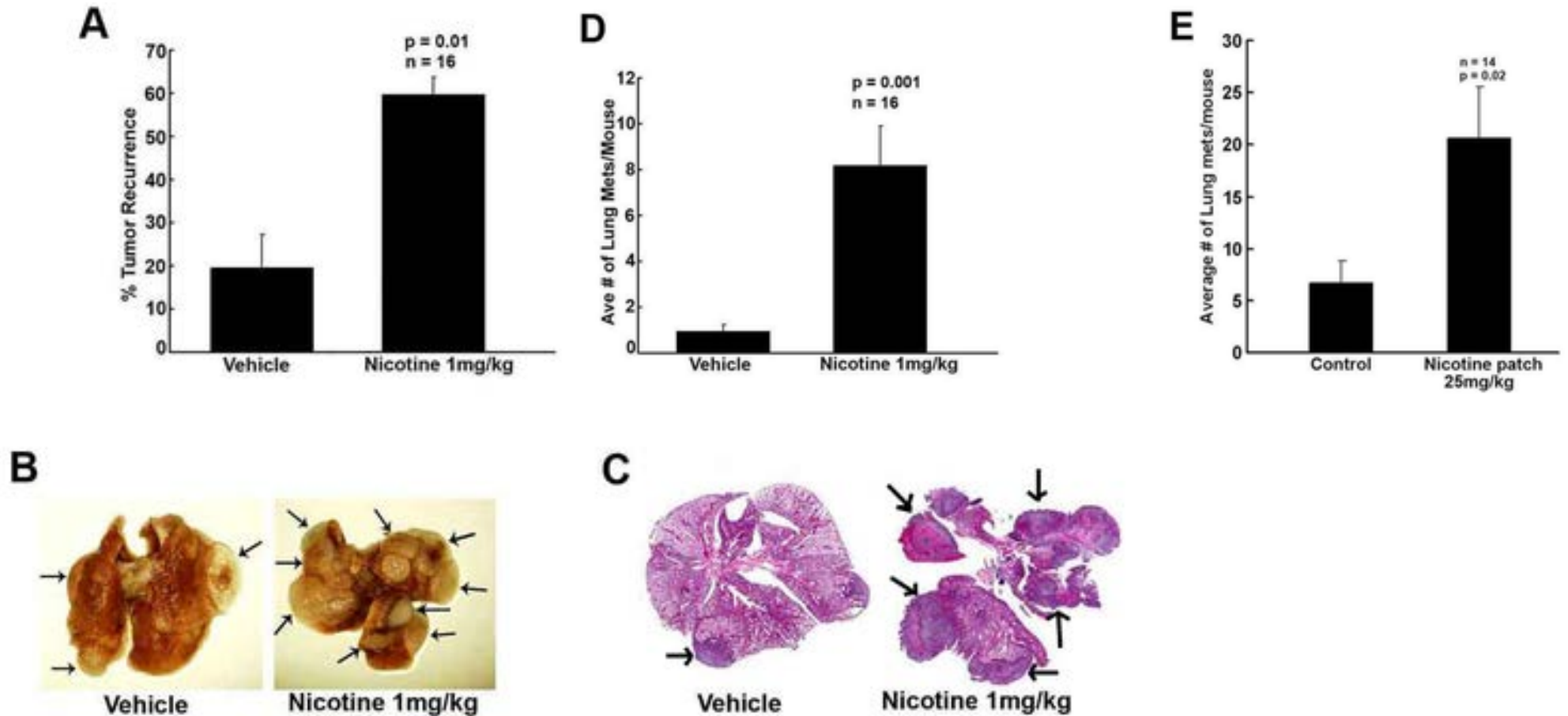
BALB/c tumor growth & metastasis *in vivo*





Results

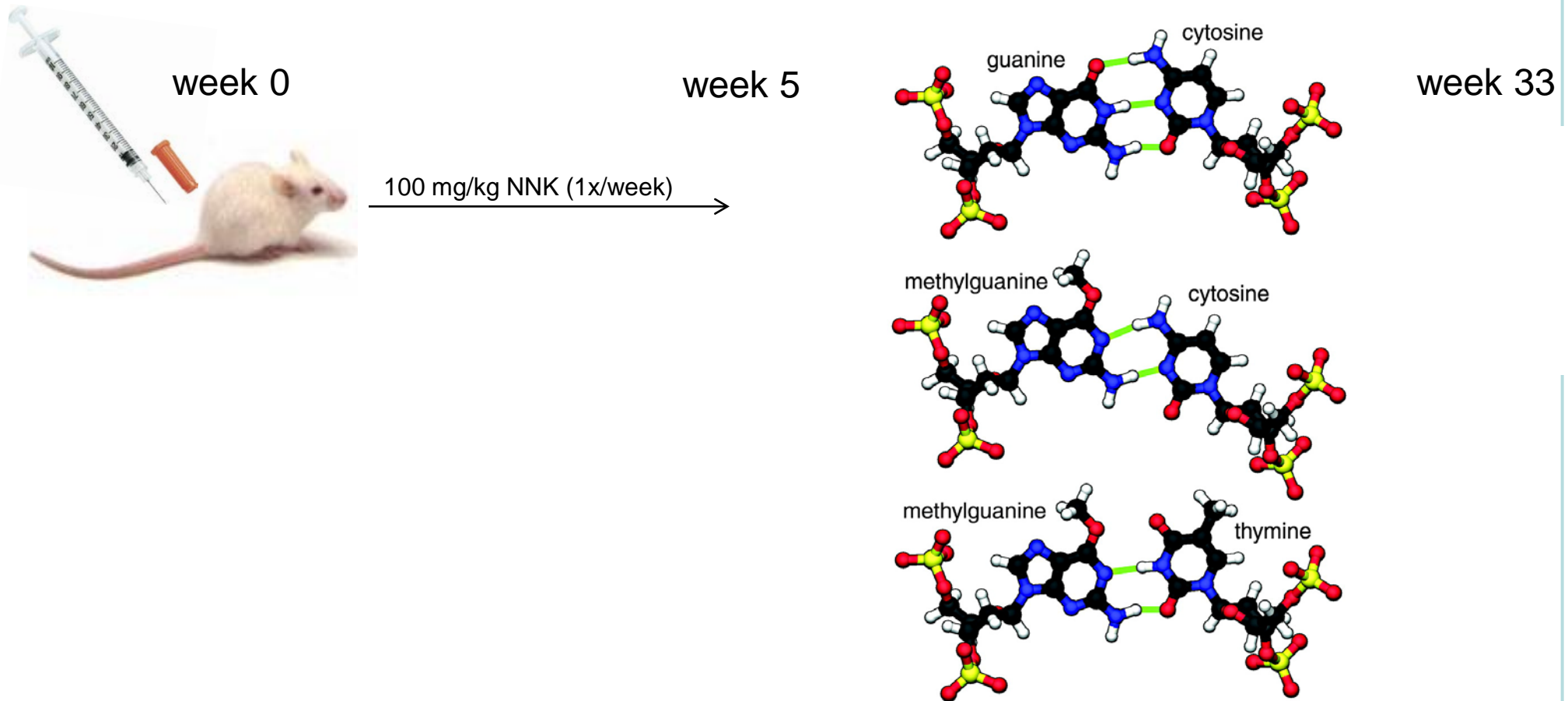
Figure 2. Nicotine increases metastatic potential.



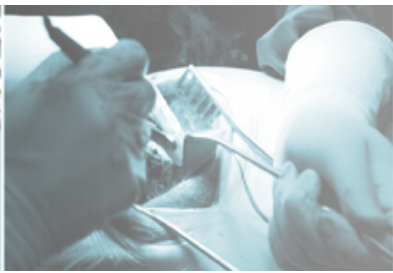
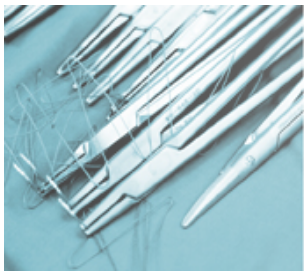


Methods

A/J tumorigenicity assay

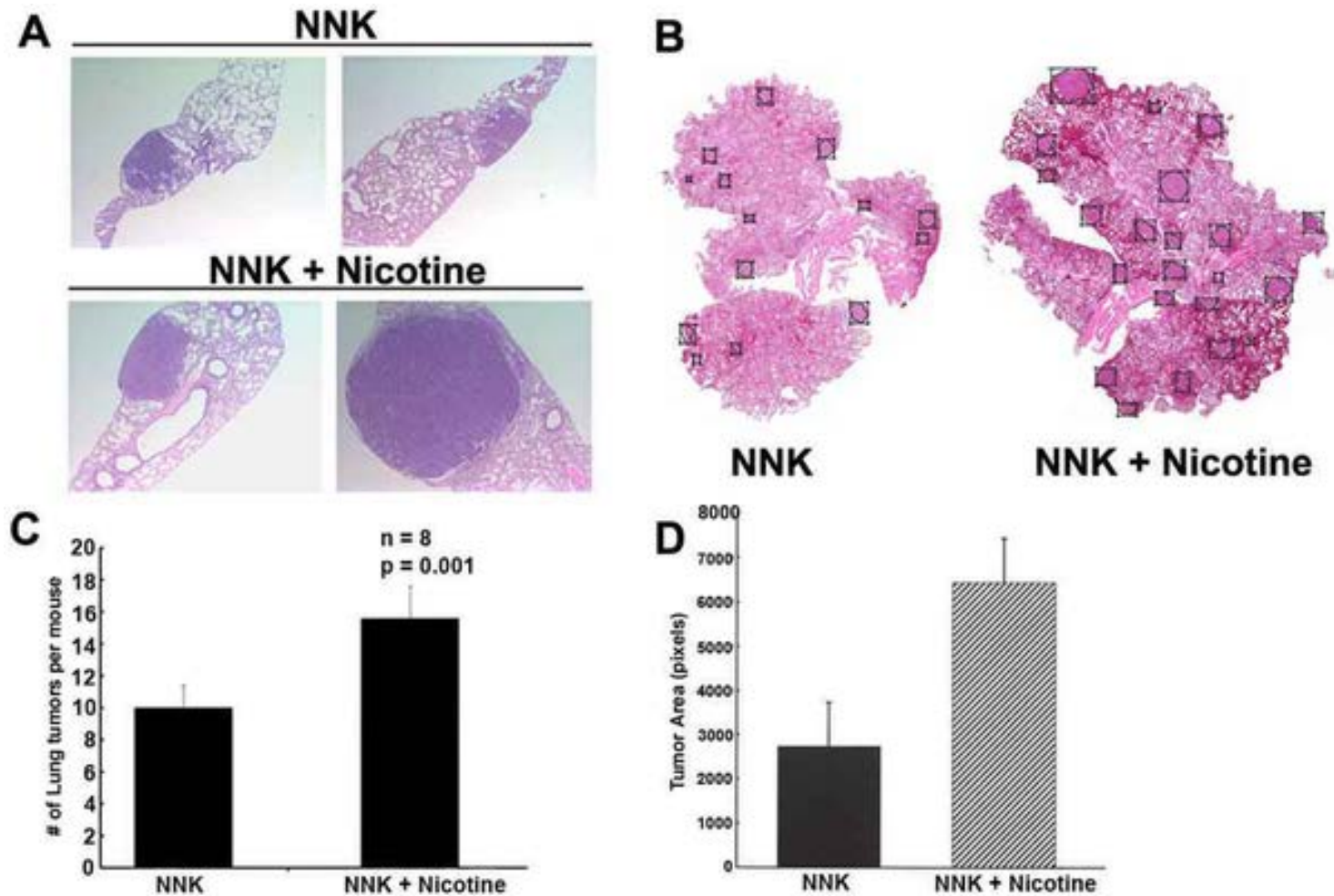


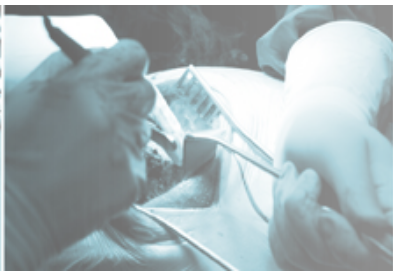
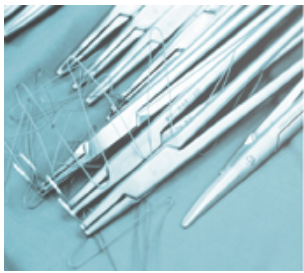
Goodsell D S *The Oncologist* 2004;9:353-354



Results

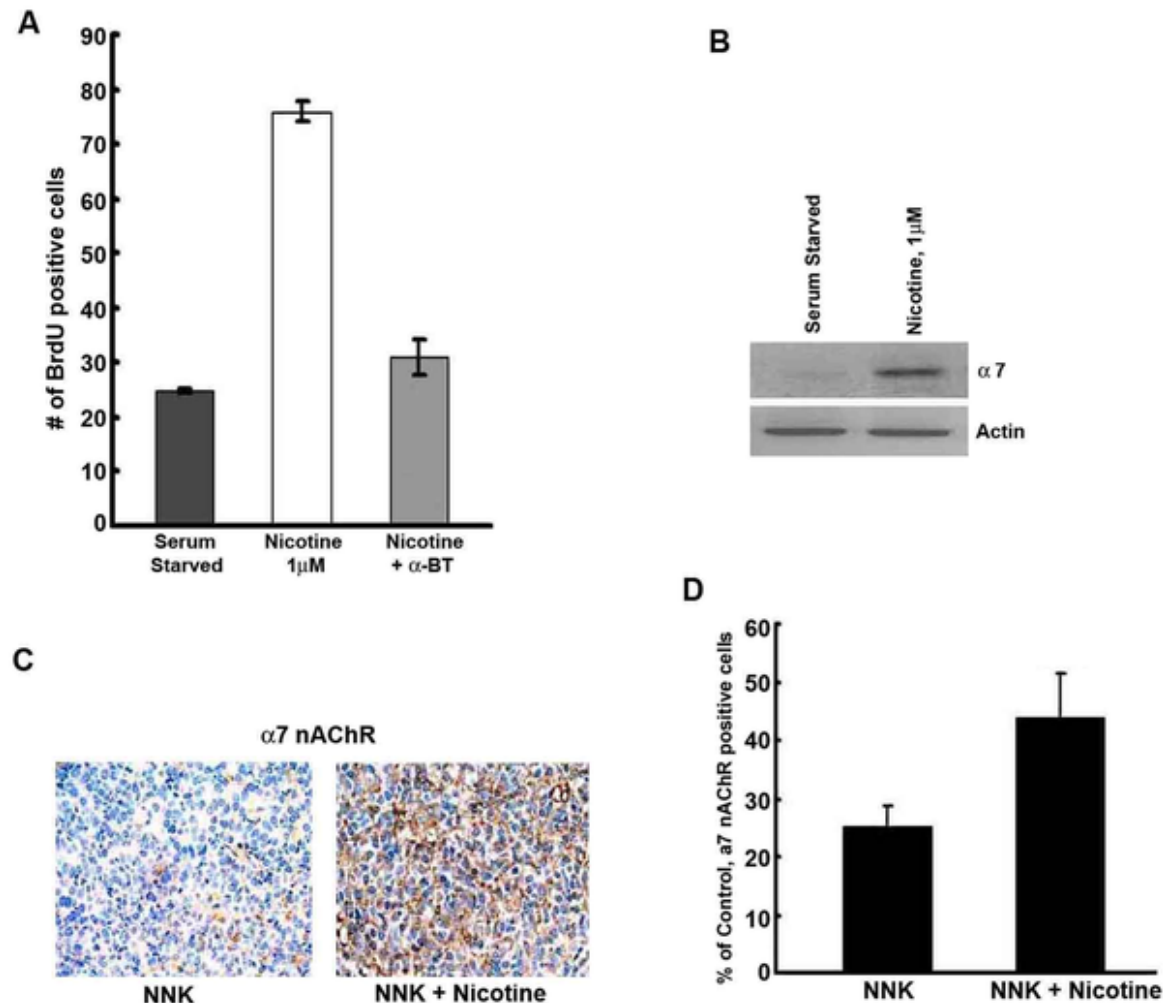
Figure 3. Nicotine increases number and size of NNK induced lung tumors.





Results

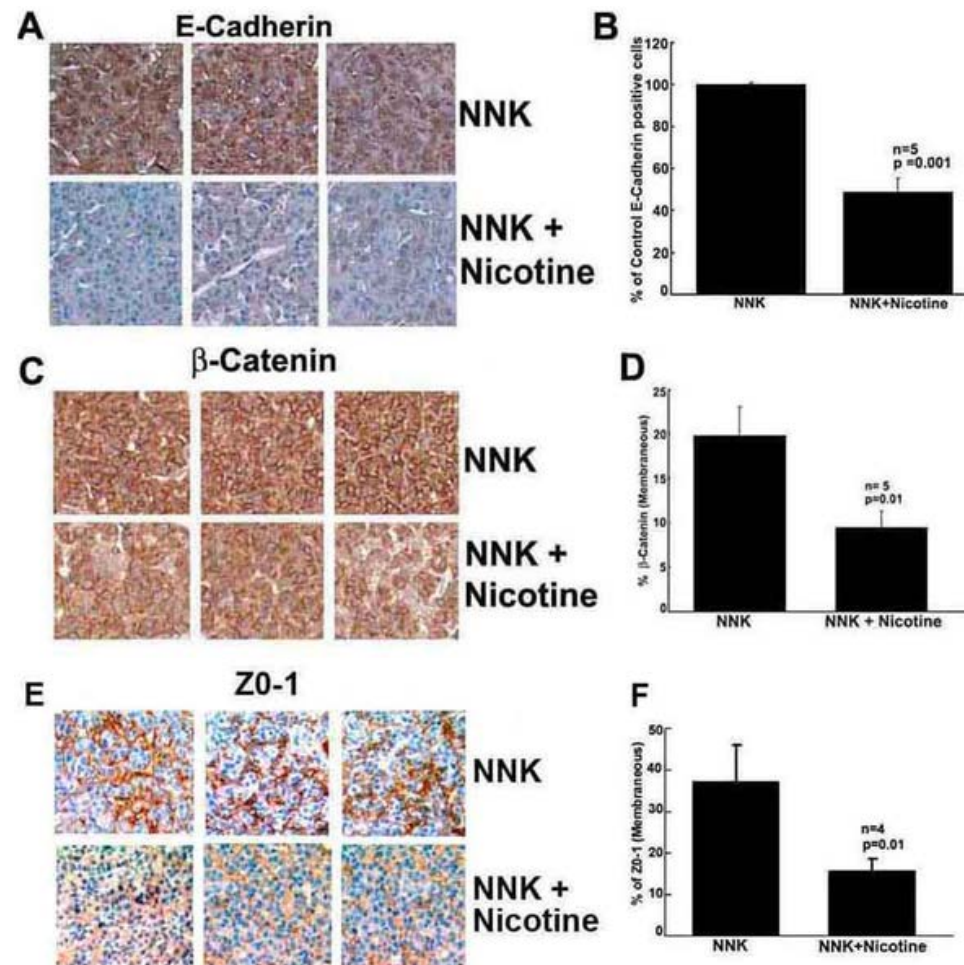
Figure 4. Nicotine enhances $\alpha 7$ nAChR subunit expression in Line1 cells.

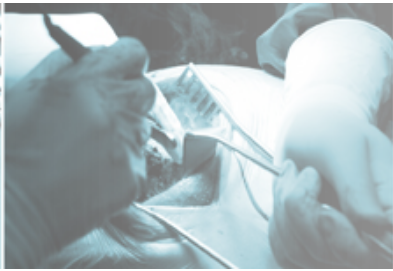
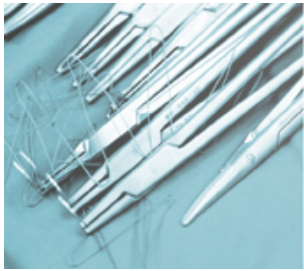




Results

Figure 5. Nicotine reduced the expression of epithelial markers in A/J mice.

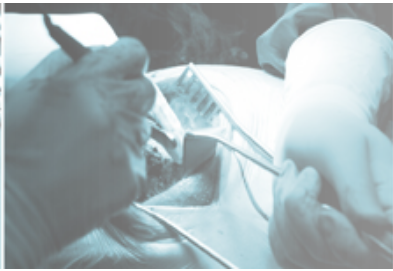
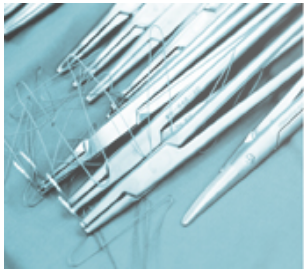




Conclusion

- Fatality of on-going smoking in cancer patients
- Promotion of tumor re-growth and metastasis via i.p. & trans-dermal nicotine





Limitations

- Cotinine levels:
 - i.p. group: 3000 ng/mL
 - patch group: 5000 ng/mL

„doses used in these studies correlated well with cotinine levels in urine of heavy smokers“
- Local recurrence
 - complete resection achieved? Histology?
- Inconsistent findings - Comparability between assays (different cell passages)