DCE-MRI Assessment of Responses to Hormonotherapy in Preclinical Breast and Prostate Cancer Models in Rats

INTRODUCTION - OBJECTIVES

Angiogenesis has been shown to be an essential factor for tumour growth and development. Recent studies have reported that estrogen regulates angiogenesis in vivo in mammary and prostate cancer models and development. Recent studies have reported that estrogen regulates angiogenesis in vivo.

Hormonal manipulation (ovariectomy, Tamoxifen treatment) inhibited the development of new mammary tumours and induced the regression of established ones in DMBA-chemoinduced breast cancer model.

METHODOLOGY

- Animals: Female Sprague Dawley rats were used for the DMBA-induced breast cancer model (induction with 20 mg/rat of DMBA given PO at D0) and male Copenhagen rats were used for the DMBA-induced prostate cancer model.

- Hemorotherapy procedure:
  - For the DMBA-induced tumour model, hormonal manipulation was performed by ovariectomy or Tamoxifen treatment (10 mg/kg, P0, Q10D28), starting at D66 after DMBA induction when 50% of rats had developed a tumour or at D86 when each rat had developed at least one tumour.
  - For the DMBA-induced prostate cancer model, hormonal deprivation was performed by castration at D97 when the mean tumour volume reached 350 mm³.

- Histological profile characterization of DMBA-induced tumours:
  - Tissue Arrays were constituted with different tumour samples excised from control or ovariectomized animals.

- DCE-MRI procedures:
  - MRI experiments were carried out on a Siemens 1.5 T Magnetom Vision. A flexible surface coil of dimensions 16x34 cm was used. During MRI, the rat was anaesthetized with a ketamine/xylazine mixture administered by intramuscular injection. The tail vein had been cannulated for contrast agent bolus administration before placing the animal in the magnet.
  - Rats were positioned in the supine position within the coil. During MRI, the rat was anaesthetized with a ketamine/xylazine mixture administered by intramuscular injection. The tail vein had been cannulated for contrast agent bolus administration before placing the animal in the magnet.
  - Rats were positioned in the supine position within the coil.

RESULTS

- Results of in vivo antitumour efficacy of hormone deprivation on DMBA-induced and R3327H tumour models:
  - Ovariectomy on DMBA-induced tumour models and development.

- Hormonal manipulation (ovariectomy, Tamoxifen treatment) inhibited the development of new mammary tumours and induced the regression of established ones in DMBA-chemoinduced breast cancer model.

- Values of tumour vascular hyperpermeability in a panel of HD and HID cancer models:

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<tr>
<th>MODEL</th>
<th>HD (K)</th>
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<tbody>
<tr>
<td>DMBA</td>
<td>0.046 ± 0.016</td>
<td>0.091 ± 0.025</td>
<td>0.255 ± 0.038</td>
<td>0.694 ± 0.142</td>
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<td>PAC120</td>
<td>0.112 ± 0.049</td>
<td>0.576 ± 0.073</td>
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<td>PC3</td>
<td>0.083 ± 0.009</td>
<td>0.270 ± 0.079</td>
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CONCLUSIONS

- Gdomer contrast agent was shown to be well suited to quantify small variations in tumour vascular permeability parameters.
- Hormone deprivation was highly effective to inhibit tumour growth in breast DMBA-chemoinduced and prostate R3327H cancer models in rats.
- Estradiol deprivation induced significant and prolonged decrease in Kpวก, ve and ve values of the castrated rats returned to the initial values that was not correlated with a regrowth of the tumours.
- Hormone withdrawal had no effects on Kpวก and ve parameters in hormonodependent (HD) breast and prostate cancer models.
- Based on these results, experiments are in progress to quantify hormone effects on hormonodependent breast tumour vascular permeability with our MRI system.

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