

# Neuroendocrine Diffuse System of the Respiratory Tract of *Rana temporaria*: An Immunocytochemical Study

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Abstract of:

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The neuroendocrine cell population of the respiratory system of *Rana temporaria* has been studied by means of immunocytochemical methods at the light-microscopic level. Isolated or clustered endocrine cells have been found in the epithelium of the buccal cavity, glottis, larynx, and lung. Nine different types of endocrine isolated cell types can be distinguished according

to their immunoreactivity to several regulatory peptides [calcitonin, substance P, bombesin, peptide histidine isoleucine (PHI), cholecystokinin (CCK), and endothelin 1] and neuroendocrine markers (7B2, chromogranin, and serotonin). Neuroepithelial bodies are innervated clusters of cells simultaneously immunoreactive for serotonin and 7B2. Nerves and/or neurons have been detected in different regions of the respiratory system using antibodies against protein gene product 9.5, serotonin, calcitonin gene-related peptide (CGRP), substance P, PHI, helodermin, and CCK.

# Cyclosporin A and doxorubicin-ifosfamide in resistant solid tumours: a phase I and an immunological study

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**Summary** In order to test whether circumvention of clinical resistance can be obtained in common solid tumours by targeting different drug resistance mechanism, a phase I clinical and immunological study was designed. The purpose of the study was to determine the dose of cyclosporin A (CsA), in combination with doxorubicin (DOX) and ifosfamide (IFX), needed to achieve steady-state whole-blood levels of 2000 ng ml<sup>-1</sup> and the associated toxicity of this combination. Treatment consisted of CsA 5 mg kg<sup>-1</sup> as a 2 h loading infusion, followed by a CsA 3 day continuous infusion (c.i.) (days 1-3) at doses that were escalated from 10

to 18 mg kg<sup>-1</sup> day<sup>-1</sup>. Chemotherapy consisted of DOX 55 mg m<sup>-2</sup> by i.v. 24 h c.i. (day 2) and IFX 2 g m<sup>-2</sup> i.v. over 1 h on days 1 and 3. Treatments were repeated every 4 weeks. Eighteen patients with previously treated resistant solid tumours received 39 cycles. Mean steady-state CsA levels  $\geq 2000$  ng ml<sup>-1</sup> were reached at 5 mg kg<sup>-1</sup> loading dose followed by a 3 day c.i. of 16 mg kg<sup>-1</sup> day<sup>-1</sup> or greater. Haematological toxicity was greater than expected for the same chemotherapy alone. One patient died of intracranial haemorrhage due to severe thrombopenia. Other observed toxicities were: asymptomatic hyperbilirubinaemia (46% cycles), mild nephrotoxicity (20% cycles), hypomagnesaemia (72% cycles), mild increase in body weight (100% cycles), hypertension (15% cycles) and headache (15% cycles). Overall the toxicity was acceptable.