# B2

## Discordant Expression of Proliferating Cell Nuclear Antigen (PCNA) and Ki-67 Antigen in Carcinoid and Pancreatic Neuroendocrine Tumors (C&PET) Likely Indicates Enhanced DNA Repair

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**Background:** Increased expression of DNA repair proteins has been implicated in chemoresistance to alkylating agents in lung, ovarian and other malignancies. We have investigated whether C&PET express high levels of these proteins potentially explaining their known *in vivo* chemoresistance.

**Methods:** We stained tumor samples from 17 patients (pts) with C&PETs of various Wick grades (four gr 1, seven gr 2 and six gr 3) for: 1. Ki-67, a marker of cell proliferation and DNA replication but not DNA repair, using MIB-1 antibody, 2. PCNA, an established DNA replication and repair biomarker (Cell 1992; 69:367-74), 3. Somatostatin receptor type 2 (SST2). The % Ki-67 and PCNA positive cells were compared between patients and correlated with the Wick grades and SST2 staining intensity.

**Results:** Median %Ki-67-positive cells was only 1.5% (range; 0.5-3%). In contrast, median %positive cells for PCNA was 90% (range; 5-100%) with 4 pts showing ≤ 50% and the remainder ≥ 60% PCNA expression. PCNA showed a characteristic staining pattern with 4+ staining of the small fraction of proliferating Ki-67-positive cells vs. 2+ to 3+ staining of quiescent cells. SST2 staining intensity was 1+ in 3, 2+ in 10 and 3+ in 4 pts with no apparent correlation between the SST2 expression and Wick grade or Ki-67 and PCNA expression. There was also no correlation between the Wick grade and Ki-67 or PCNA expression.

**Conclusions:** This is the first demonstration of a very high expression of PCNA in C&PET that is clearly discordant with cellular proliferation/Ki-67 expression. This finding likely indicates enhanced DNA repair in most C&PET and may explain their general *in vivo* chemoresistance. Further studies with other DNA replication and repair biomarkers such as thymidine kinase 1 (TK1), replication protein A (RPA), and excision repair cross-complementation group 1 (ERCC1) are ongoing.