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Comment on: 'COUP-TFII regulates metastasis of colorectal adenocarcinoma cells by modulating Snail1'

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Sir,

We read with great interest the paper by Bao *et al* (2014) entitled 'COUP-TFII regulates metastasis of colorectal adenocarcinoma cells by modulating Snail1', showing upregulation of Snail and down-regulation of E-cadherin in the human epithelial intestinal cell line HIEC overexpressing COUP-TFII upon transfection (Bao *et al*, 2014; Figure 5) and converse effects in COUP-TFII-KO loVo cells (Bao *et al*, 2014; Figure 4). We previously explored the role of COUP-TFII as a regulator of E-cadherin expression because we also had noticed a correlation between abnormally high expression of COUP-TFII and lack of E-cadherin in a large panel of carcinoma cell lines of various origins including 22 colon cancer cell lines. We transfected several cell lines with an inducible COUP-TFII expression vector and, as shown in Figure 1, did not observe a pronounced effect on E-cadherin expression. In the human colon carcinoma line HCT116 in particular, E-cadherin remained perfectly stable. HCT116 cells are not invasive in Matrigel assays and invasion was not induced by COUP-TFII. Importantly, in the lung carcinoma line A549 that is invasive straightaway, E-cadherin expression was moderately increased together with, as previously reported (Navab *et al*, 2004), the invasion capacity of the cells. We also extinguished COUP-TFII expression in E-cadherin-negative cell lines (SW800, MDA-MB 231) using RNA interference and saw no E-cadherin switch-on. Together with the data from Bao *et al*, this shows that the effect of COUP-TFII is highly dependent on the cellular context. This is actually not very surprising since transcriptional regulation by COUP-TFII is quite complex, involving dimerisation and recruitment of cofactors, and can encompass not only activation but also direct and indirect repression (Park *et al*, 2003).

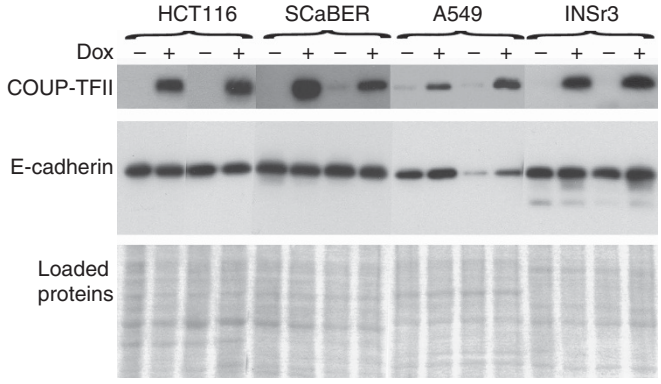

Figure 1. Expression of E-cadherin in cell lines overexpressing COUP-TFII upon transfection. HCT116 (human colon carcinoma), SCaBER (human bladder squamous carcinoma), A549 (human lung carcinoma) and INS (rat insulinoma) cell lines were treated with doxycyclin (+) to induce COUP-TFII expression. Two different clones are shown for each transfected cell line. COUP-TFII and E-cadherin expression was evaluated by western blotting using 20 μg of total protein extracts. Equal loading was checked by staining the membrane with amidoblack.

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Comment on 'Updated investigations of cancer excesses in individuals born or resident in the vicinity of Sellafield and Dounreay': premature all-clear for nuclear power

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Sir,

Bunch *et al* (2014) report no increased leukaemia/cancer rates in children and young adults below age 25 in Seascale ward near the Sellafield nuclear site, during the period 1991–2006. But the case numbers are very small – 1 observed leukaemia case ($O=1$) *vs* 0.26 expected cases ($E=0.26$), which means a standardised incidence ratio (SIR) of 3.9 with a wide 90% confidence interval (90% CI: 0.28–33.8). Near the Dounreay nuclear installation, in the wards of Thurso and Reay, not a single leukaemia case was registered in 1991–2006, and also not in the respective control region, the rest of Caithness county. Thus, for 1991–2006, no meaningful conclusions about leukaemia risk near Sellafield and Dounreay can be drawn from these numbers.

Bunch *et al* fail to discuss the leukaemia increases over the full period, 1963–2006. A highly significant increase is found in Seascale ward ($O=6$, $E=0.91$, SIR = 6.67, 90% CI: 2.9, 13.0). The ratio of the SIR in Seascale (SIR = 6.67) to the SIR in Copeland and Allerdale County excluding Seascale (SIR = 0.90) yields a relative risk (RR) of RR = 6.67/0.90 = 7.4 ($P=0.0002$). Near Dounreay the increase in leukaemia risk is not significant (RR = 1.64, $P=0.227$). For all malignancies and over the whole study period 1963–2006 a significantly increased risk is found near Sellafield (RR = 3.3, $P=0.0004$), but the increase is not statistically significant near Dounreay (RR = 1.22, $P=0.274$).

Pooled data from Sellafield, Dounreay, and La Hague: Guizard *et al* (2001) reported on leukaemia around the La Hague reprocessing plant in France between 1978 and 1998. Leukaemia rates in the 10-km zone were compared with rates in the 10–35-km zone. During the 21-year study period, four leukaemia cases were found among children in the 10-km