LINK TO ORIGINAL ARTICLE

The integrin signalling adaptor p130CAS is also a key player in prostate cancer

Gaelle Fromont and Olivier Cussenot

In a recent Review article (Integrin signalling adaptors: not only figurants in the cancer story. *Nature Rev. Cancer* **10**, 858–870 (2010))[1], Sara Cabodi and colleagues discussed the influence of integrin adaptors, including the p130 Crk-associated substrate (p130CAS; also known as BCAR1) in cancer cell transformation and tumour progression. The authors discussed the growing body of evidence that supports a central role for p130CAS in acquired resistance to hormonal treatment for breast cancer. They also pointed out that investigation of p130CAS in human tumours was limited to breast cancer and haematological malignancies. In breast cancer, high p130CAS expression was shown to correlate with disease progression and resistance to tamoxifen, and p130CAS increases oestrogen-dependent signalling in breast cancer cells *in vitro* by associating with oestrogen receptor-α. Breast and prostate cancer share numerous biological similarities, including dependence on steroid hormones, both androgens and oestrogens, for growth and survival. However, results concerning the involvement of p130CAS in prostate cancer were not discussed[1].

Biological similarities in hormone deprivation-resistance pathways in breast and prostate cancers involving p130CAS have previously been reported[2,3]. Indeed, we have shown that p130CAS expression in prostate cancer is associated with disease aggressiveness and progression[2]. p130CAS staining was present in only 15% of low-grade localized prostate cancers, in 48% of high-grade localized tumours, in 60% of lymph node metastasis and in 80% of castration-resistant prostate cancers[2]. p130CAS expression was also associated with high epidermal growth factor receptor (EGFR) expression and reduced expression of the metastasis suppressor gene *CD82* (also known as *KAI1*)[2]. Moreover, *in vitro* studies showed that reduced levels of p130CAS in the DU145 prostate cancer cell line are largely responsible for CD82-induced suppression of cell motility[3]. In addition, the Src family kinase inhibitor saracatinib (also known as AZD0530) has been shown to inhibit p130CAS phosphorylation in DU145 and PC3 prostate cancer cell lines and to quickly decrease cell migration[4].

Sara Cabodi and colleagues also reported that the protein tyrosine phosphatase regenerating liver (PRL3; also known as PTP4A3) reduces p130CAS cleavage and is therefore a crucial regulator of p130CAS protein levels. *PTP4A3* is located at chromosome 8q24, which is frequently amplified in advanced and metastatic prostate cancer[5]. Regarding the relationship between p130CAS and resistance to hormone treatment, we recently demonstrated that p130CAS expression in prostate cancer tissues was associated with a shorter time to relapse after androgen-deprivation therapy, and was therefore a good predictor of tumour progression after castration[6].

Taken together, these data suggest that p130CAS expression could have clinical implications for prostate cancer, as it may improve the classification of patients into different prognostic groups, enabling more individualized treatment approaches. The involvement of p130CAS in prostate cancer progression and acquired resistance to castration make it a suitable target for new therapeutic avenues.

Gaelle Fromont and Olivier Cussenot are at the Centre d'etude et de Recherche sur les Pathologies Prostatiques (CeRePP), Paris 75020, France.

Gaelle Fromont is also at the Department of Pathology, Centre Hospitalier Universitaire, Universite de Poitiers, Poitiers 86000, France.

Olivier Cussenot is also at the Department of Urology, Hopital Tenon, Universite Pierre et Marie Curie, Paris 75020, France

Correspondence to G.F.
e-mail: g.fromont@chu-poitiers.fr

doi: 10.1038/nrc2967-c1

1. Cabodi, S., Camacho-Leal, M. D. P., Di Stefano, P. & Defilippi, P. Integrin signalling adaptors: not only figurants in the cancer story. *Nature Rev. Cancer* **10**, 858–870 (2010).
2. Fromont, G., Vallancien, G., Validire, P., Levillain, P. & Cussenot, O. BCAR1 expression in prostate cancer: association with 16q23 LOH status, tumor progression and EGFR/KAI1 staining. *Prostate* **67**, 268–273 (2007).
3. Zhang, X. A., He, B., Zhou, B. & Liu, L. Requirement of the p130^{CAS}-Crk coupling for metastasis suppressor KAI1/CD82-mediated inhibition of cell migration. *J. Biol. Chem.***18**, 27319–27328 (2003).
4. Chang, Y. M. *et al.* Src family kinase oncogenic potential and pathways in prostate cancer as revealed by AZD0530. *Oncogene* **27**, 6365–6375 (2006).
5. Liu, W. *et al.* Homozygous deletions and recurrent amplifications implicate new genes involved in prostate cancer. *Neoplasia* **10**, 897–907 (2008).
6. Celhay, O. *et al.* Expression of estrogen related proteins in hormone refractory prostate cancer: association with tumor progression. *J. Urol.* **184**, 2172–2178 (2010).

Competing interests statement
The authors declare no competing financial interests.