

# Expression of p120-catenin isoforms correlates with genomic and transcriptional phenotype of breast cancer cell lines

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**Abstract.** *Background:* P120-catenin is a member of the Armadillo protein family, which is involved in intercellular adhesion and cell signalling. It directly interacts with the classical cadherins juxtamembrane domain and contributes for both junction formation and its disassembly. Accumulating evidences indicate that p120-catenin is important in tumour formation and progression, although the role of their multiple spliced isoforms in the regulation of cadherin-mediated adhesion of malignant cells is still not well understood. We investigated the expression of p120-catenin isoforms in a collection of breast cancer cell lines with distinct molecular profiles and expressing different cadherins. *Methods:* We assessed the expression by RT-PCR and Western-blotting analysis. *Results:* We observed that the expression of p120-catenin isoforms was associated with the genomic and transcriptional phenotype of breast cancer cells. Besides, the recruitment of p120-catenin isoforms was not apparently related with the particular expression of E-, P- or N-cadherin. *Conclusion:* We demonstrate that mammary tumour cells exhibit a characteristic p120-catenin isoform expression profile, depending from their specific genomic and transcriptional properties. These particular expression patterns, combined with other regulatory proteins and in a specific cellular context, may explain how p120-catenin can either contribute to strength intercellular adhesions or instead to promote cell motility.

**Keywords:** Breast cancer cells, cadherin, cell–cell adhesion, p120-catenin isoforms

## 1. Introduction

Cadherins are transmembrane proteins which mediate calcium-dependent cell–cell interactions, playing an important role in tissue organization during embryogenesis as well as in adult organisms [1–3]. Classical cadherins, such as E-, N- and P-cadherin, are the best characterized adhesion proteins, exhibiting three distinct molecular domains (extracellular, transmembrane and cytoplasmic) and promoting mainly homophilic

and homotypic interactions [4,5]. The function and strength of cadherin-mediated adhesion depend on dynamic association with a group of cytoplasmic molecules, called catenins, which ensure the linkage of cadherin cytoplasmic tail to the actin cytoskeleton [6]. These cytoplasmic partners include  $\beta$ - and  $\gamma$ -catenin (or plakoglobin), which in turn bind  $\alpha$ -catenin that interacts directly or indirectly with the actin filament network [7]. P120-catenin (p120ctn) is an additional catenin that is rising as an important contributor for the regulation of cadherin adhesive activity.

P120ctn belongs to the Armadillo protein family, which is characterized by a central Arm-repeat domain that directly interacts with cadherins [8]. This molecule is encoded by *CTNND1* gene on the chromosome 11q11 [9], and it was originally identified as a *Src* substrate [10]; later it was shown to interact with the highly conserved cadherin juxtamem-

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brane domain (JMD) [8]. Owing to alternative splicing and multiple translation initiation codons, multiple p120ctn isoforms can be expressed from a single gene (Fig. 1A) [9]. N-terminal splicing events lead

to the use of four different start codons, resulting in the expression of p120ctn isoforms type 1, 2, 3 or 4, according to the respective ATG used as the translation start site. However, intra and interexonic splicing

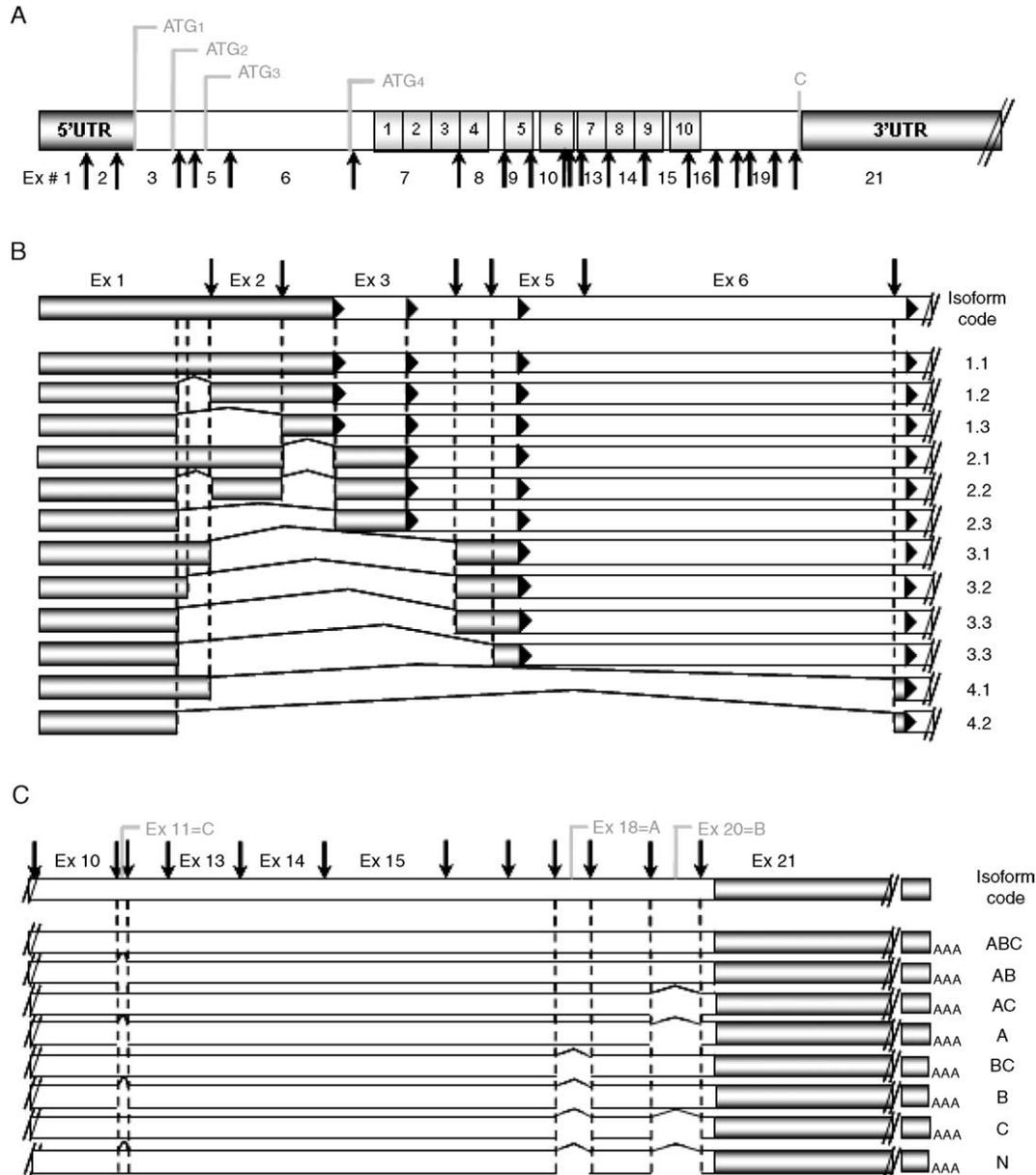


Fig. 1. Schematic diagram of the human p120ctn gene (*CTNND1*) and from the multiple alternatively spliced isoforms. (A) Structure of *CTNND1* gene. ATG<sub>1-4</sub> represent the positions of the four alternatively used start codons; C is the position of the stop codon; numbered boxes (1 to 10) correspond to the encoding sequences of Armadillo repeats; exons are indicated by numbers (1 to 21), separated by vertical arrows. (B) Schematic representation of the various isoforms generated by alternative splicing in 5' region of *CTNND1* gene. Vertical arrows separate each exon, and triangles represent the four different start codons that can be alternatively used. The codes for the encoded protein isoforms are shown on the right. (C) Schematic representation of the alternatively used exons in 3' region of *CTNND1* gene. Exons are separated by vertical arrows, triangle corresponds to the stop codon and a poly(A) addition site is also represented (AAA). The codes for the encoded protein isoforms are shown on the right (adapted from [9]).

events in this 5' region of the p120ctn mRNA generate twelve different transcript isoforms, termed 1.1, 1.2, 1.3, 2.1, 2.2, 2.3, 3.1, 3.2, 3.3, 3.4, 4.1 and 4.2, where isoform 1.1 corresponds to the full-size mRNA variant (Fig. 1B). Alternative splicing events also occur in the C-terminal end, leading to the use of exons A, B, C or none of them (Fig. 1C). Therefore, various combinations of these N- and C-terminal exons predict up to 32 isoforms of human p120ctn, although several of these possible splicing combinations may not exist *in vivo* [9]. In addition, differential posttranslational modifications could further increase the molecular variety of these proteins, since they could be phosphorylated on serine/threonine and tyrosine residues by several protein kinases [11].

Once p120ctn binds to the cadherin JMD, it has been proposed to regulate cadherin adhesive activity, either positively or negatively [12]. In fact, p120ctn may act as a switch that induces cadherin clustering and strong adhesion when activated [13,14], or junction disassembly following signalling events leading to its inactivation [15,16]. According to this, two recent reports showed that p120ctn acts as a rheostat, controlling the cadherin levels in a cell-context-dependent-manner [17], as well as promoting a sessile cellular phenotype when associated with E-cadherin or a motile phenotype when associated with mesenchymal cadherins (such N-cadherin, cadherin-11 or R-cadherin) or with P-cadherin [18,19]. P120ctn may also modulate cell-cell adhesion by influencing the actin cytoskeleton organization and the Rho-family GTPases activity [20]. This molecule was still proposed as a promoter of the cadherin cell surface trafficking through the recruitment of kinesin [21] and, similarly to the other catenins, it can translocate into the cell nucleus [22], where it binds to the transcription repressor Kaiso [23,24]. The implication of p120ctn in the regulation of cadherin function seems to be important not only in embryonic morphogenesis, but also in the process of tumour formation and progression. Indeed, p120ctn altered expression or delocalization has been observed in various human tumours [25]. Interestingly, human tumour cell lines exhibited a highly heterogeneous p120ctn isoform expression pattern [26], which could contribute to cadherin failure or explain differences in morphological or invasive behaviour of malignant cells. For example, a study in pancreatic cancer cells demonstrated that shorter and unphosphorylated p120ctn isoforms were linked to E-cadherin expression, whereas longer and tyrosine phosphorylated isoforms were more related with N-cadherin [27].

We are particularly interested in clarifying the role of p120ctn in the mediation of cadherin function in different types of breast carcinomas. This disease is extremely heterogeneous, encompassing tumours distinct in behaviour, outcome and response to therapy. Microarray technology allowed the grouping of breast carcinomas in five main categories, according to their expression profiles and clinical courses [28]. A very recent report described an identical analysis in a collection of breast cancer cell lines, establishing three main gene clusters that mirror several genomic and molecular properties found in primary breast tumours: Luminal (*ERBB3*- and *ER*-positive), Basal A (*ER*-negative, *CAVI*-, *KRT5*- and *KRT14*-positive) and Basal B (*ER*-negative, *CAVI*- and *VIM*-positive) [29].

This present study is the first investigating the expression of p120ctn isoforms in a collection of human breast cancer cell lines with distinct molecular profiles and expressing different cadherins. We screened the cadherin and p120ctn isoforms expression profile of a breast cancer cell line collection. We found that mammary cancer cell lines exhibit an interesting cell-type-specific expression pattern of p120ctn isoforms, which is associated with particular genomic and transcriptional properties of each cell line.

## 2. Materials and methods

### 2.1. Cell culture

Human breast cancer cell lines were obtained from the ATCC or from collections developed in the laboratories of Drs Elena Moisseva (Cancer Biomarkers and Prevention Group, Departments of Biochemistry and Cancer Studies, University of Leicester, UK), Marc Mareel (Laboratory of Experimental Cancerology, Ghent University Hospital, Belgium) and Eric Lam (Imperial College School of Medicine, Hammersmith Hospital, London, UK). Cell lines were organized according to the very recent classification proposed by Neve et al. [29], which defined three gene clusters termed Luminal, Basal A or Basal B. All the cell lines were grown in commercially available medium (50%DMEM/50%Ham's F12 for MCF-7/6 and MCF-7/AZ; RPMI for ZR-75.1; DMEM for MCF-7 (ATCC), T47D, Hs 578T, BT-474, BT-549, SkBr3 and HBL-100; MEM for BT-20;  $\alpha$ -MEM for MDA-MB-231, MDA-MB-435 and MDA-MB-468), supplemented with 10% heat-inactivated Fetal Bovine serum (FBS, Invitrogen, Carlsbad, CA) and with 1%

antibiotic solution (penicillin–streptomycin, Invitrogen). In addition, ZR-75.1 cells were also supplemented with 1 nM 17 $\beta$ -estradiol (Sigma Aldrich Corp., St. Louis, MO). All lines were routinely cultured in a humidified atmosphere with 5% CO<sub>2</sub> and at 37°C. When cells reached 70–80% confluence, RNA and protein cell lysates were isolated.

## 2.2. Reverse transcription (RT)-PCR analysis

Total RNA was extracted from approximately 4 × 10<sup>6</sup> cells using RNeasy Mini Kit (Qiagen, Hilden, Germany) following the manufacturer's instructions. One microgram of total RNA was reverse transcribed to single-stranded cDNAs with oligo(dT) primers using the Omniscript Reverse Transcriptase procedure (Qiagen). The obtained cDNA was subsequently used for PCR amplification of E-, P- and N-cadherin, GAPDH (used as internal control), total p120ctn and its several isoforms. Primer pairs were previously reported

in three studies [9,30,31] and are listed in Table 1. The standard 25  $\mu$ l PCR mixture contained 1x PCR buffer, 1.5 mM MgCl<sub>2</sub>, 200  $\mu$ M dNTPs, 0.5  $\mu$ M of each primer, 1U Taq DNA polymerase (Fermentas International Inc., Burlington, CA), distilled water and 200 ng cDNA template. Additionally, we used Platinum Taq DNA polymerase (Invitrogen) to amplify higher fragments. PCR reactions were performed in thermal cyclers (MyCycler, Bio-Rad Laboratories, Amadora, Portugal) with an initial denaturation at 94°C for 3 minutes, 30 or 35 cycles of 94°C for 30 seconds (denaturation), 50 seconds at the specific primer annealing temperature (Table 1), and 72°C for 1 minute (elongation), and a final extension at 72°C for 10 minutes. Negative controls without cDNA were used for all sets of PCRs. The products were analysed on a 2% agarose gel and compared to a 50- or 100-bp DNA ladder (Fermentas).

Table 1

Sequences of the primers used to amplify E-, P- and N-cadherin transcripts, total p120ctn mRNA and its several spliced alternative isoforms. Primers to amplify GAPDH mRNA, as an internal control, were also used

Primer set <sup>1</sup>	Sequence 5' → 3'	T <sub>A</sub> (°C) <sup>2</sup>	Fragment size (bp)
E-cadherin:			
E-cad F	TCTACAGCATCACTGGCCAAGGAGCTG	65	475
E-cad R	AGCTTGAACCACCAGGGTATACGTAGG		
P-cadherin:			
P-cad F	ACGAAGACACAAGAGAGATTGG	55	308
P-cad R	CTATGATGGAGATGTTTCATGG		
N-cadherin:			
N-cad F	TGCGGTACAGTGTAAGTGGCCAGG	65	438
N-cad R	CGATCAAGTCCAGCTGCCACTGTG		
Total p120ctn:			
Ex7F1	CAGCATGAGCGAGGAAGTTT	55	540
Ex8R1	ATGGCGTGGCTTACAGTCTT		
Isoforms 1, 2, 3:			
Ex1F6	TGCCCTGCTGGATTTGTCTT	56	778 (1.1), 705 (1.2), 586 (1.3), 669 (2.1), 596 (2.2), 477 (2.3), 369 (3.1), 319 (3.2), 297 (3.3), 225 (3.4)
Ex5R1	CGAGTGGTCCCATCATCTG		
Isoforms A, B:			
Ex18F1	AAACCTGATCGGGAAGAAAT	52	470 (A), 557 (B)
Ex21R3	ACTGGCAAAAAGAACTAATC		
Isoform C:			
Ex10F2	TTGCCTTCTTCGGAATTAT	52	193
Ex12R1	CACTGTATCGTTTGTCTGGAT		
GAPDH:			
GAPDH F	GGTCATCCCTGAGCTGAACG	58	294
GAPDH R	TTCGTTGTCATACCAGGAAAT		

<sup>1</sup>Primer names refer to their specificity (Ex, exon number) and their sense (F, forward) or antisense (R, reverse) orientation.

<sup>2</sup>Annealing temperatures for the different PCRs.

2.3. Western blotting analysis

Cells were lysed with PBS containing 1% Nonidet-P40 (Sigma) and 1:7 Protease Inhibitors Cocktail (Roche Diagnostics GmbH, Mannheim, Germany). Protein concentration was determined by Bio-Rad protein assay (Bio-Rad, Richmond, CA) and equal amounts were resolved on a 6% denaturing polyacrylamide gel and transferred onto a nitrocellulose membrane (Amersham Pharmacia Biotech, Piscataway, NJ). After blocking nonspecific binding with 5% non-fat dry milk in PBS containing 0.5% Tween 20, each membrane was incubated for 1 hour at room temperature with each of the following primary antibodies: anti-p120ctn (clone 98, Transduction Labs, Lexington, KY, 1:1000), anti-E-cad (clone HECD-1, TaKaRa Biochemicals Inc., Kyoto, Japan, 1:500), anti-P-cad (clone 56, Transduction Labs, 1:500) or anti-N-cad (clone GC-4, Sigma, 1:500). Anti- $\alpha$ -tubulin (clone DM1A, Sigma, 1:10000) was used in all the blots as a loading control. After washing four times with PBS for 5 minutes, the membranes were incubated with a donkey anti-mouse IgG peroxidase-conjugated secondary antibody (Santa Cruz Biotechnology, Inc., Heidelberg, Germany, 1:10000) for 45 minutes and washed six more times for 5 minutes. Detection was assessed using the ECL chemiluminescence detection kit (Amersham).

3. Results

3.1. mRNA expression of E-, P- and N-cadherin and total p120ctn in breast cancer cell lines

Initially, we investigated the mRNA expression levels of the major classical cadherins (E-, N- and P-cadherin) and the total p120ctn among the different breast cancer cell lines, by RT-PCR analysis (Fig. 2). We observed that E-cadherin mRNA was essentially expressed by both Luminal and Basal A cell lines, but it was not observed in Basal B group. In contrast, N-cadherin transcripts were restricted to Basal B cell lines, being completely absent from the other groups of cells. P-cadherin transcripts were predominantly detected in Basal A group, being also present in almost all Luminal and in only one Basal B cell line (BT-549). Concerning total p120ctn mRNA, it was observed in all the cell lines tested. Interestingly, the Luminal breast cancer cell line SkBr3 did not express any of the cadherins we studied, but it displayed p120ctn transcripts.

3.2. mRNA expression of p120ctn isoforms in breast cancer cell lines

After analysing the cadherin and total p120ctn transcripts expression profile of the entire breast cancer cell lines collection, we analysed the mRNA expression of the several p120ctn isoforms, using primers that covered both 5' and 3' region of the coding sequence.

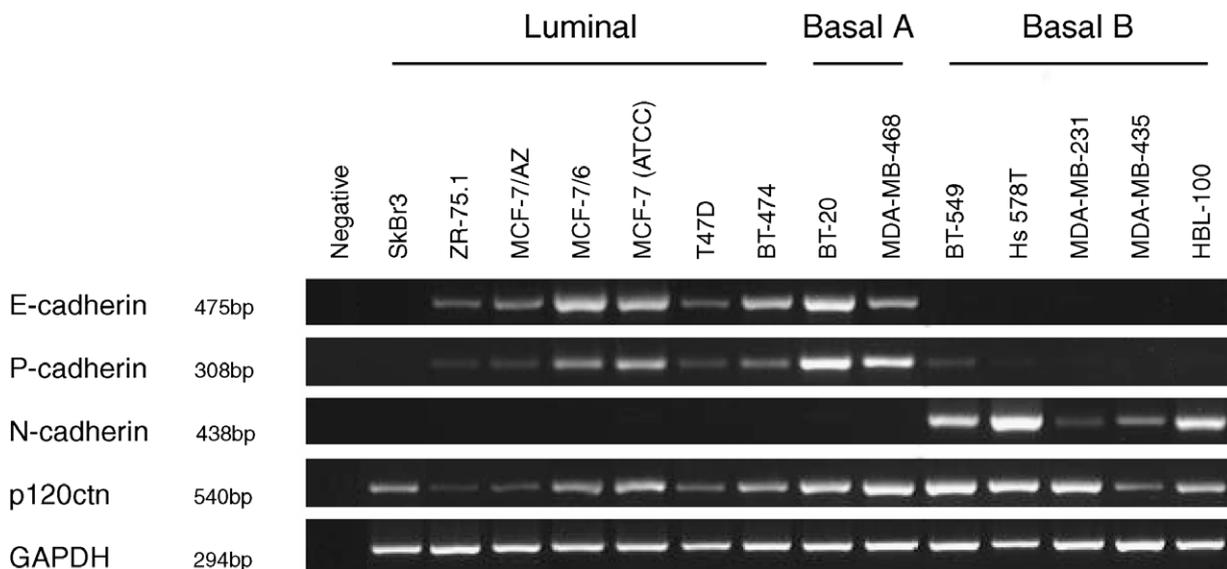


Fig. 2. Expression profile of E-, P- and N-cadherin and total p120ctn transcripts of breast cancer cell lines, analysed by RT-PCR. The different fragment sizes are indicated on the left. GAPDH expression was used as internal control.

Relatively to the 5' region, we could find several bands in the agarose gel electrophoresis (Fig. 3), which correspond to different mRNA variants of isoforms type 1, 2 and 3. Generally, isoforms type 3 (including 3.1, 3.2, 3.3 and 3.4 variants) were detected in all the cell lines studied, whereas the longest mRNA variant 1.1 was not identified in anyone. Considering the cellular genomic phenotype, we observed that Luminal cell lines mainly expressed type 3 isoforms, but they also exhib-

ited type 2.2 and 2.3 variants in lower amounts and did not display transcripts of type 1 isoforms. Contrarily, these long variants were frequently observed in Basal B cell lines, which also displayed all the other types of p120ctn isoforms. These data reveal that the expression of p120ctn isoforms is specific from a cell type, with particular genomic and transcriptional characteristics.

Relatively to the 3' region of the p120ctn coding sequence (Fig. 4), we observed that exon C is tran-

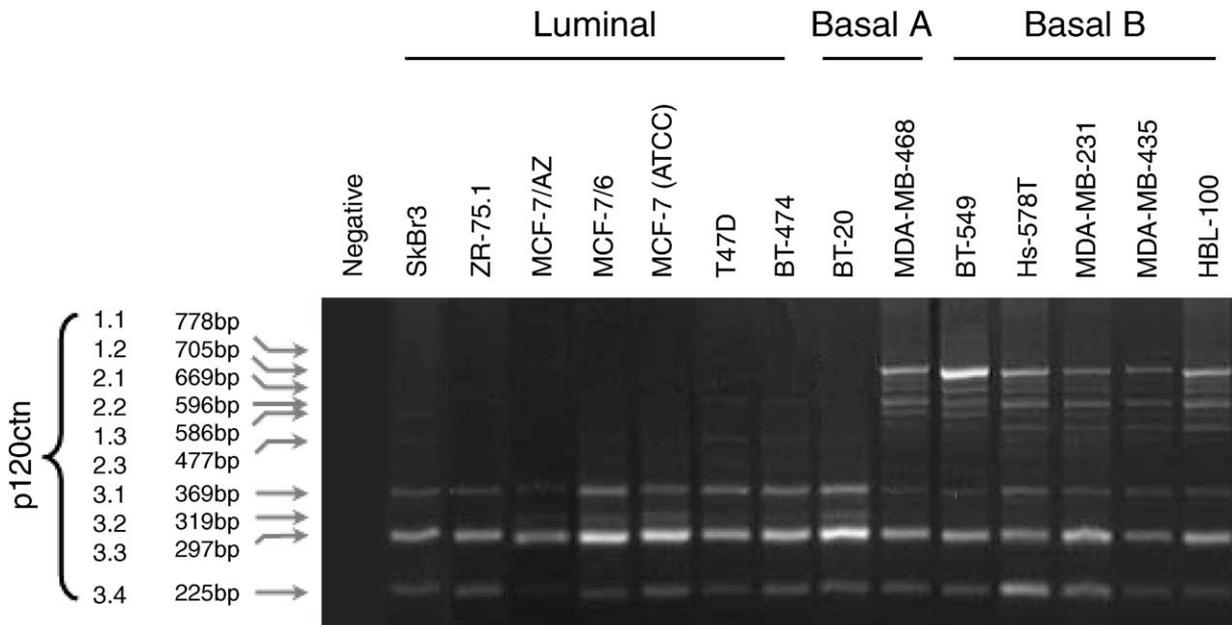


Fig. 3. Expression of p120ctn isoforms type 1, 2 and 3 mRNAs in breast cancer cell lines, analysed by RT-PCR. Numeric isoform codes and their fragment sizes are depicted on the left.

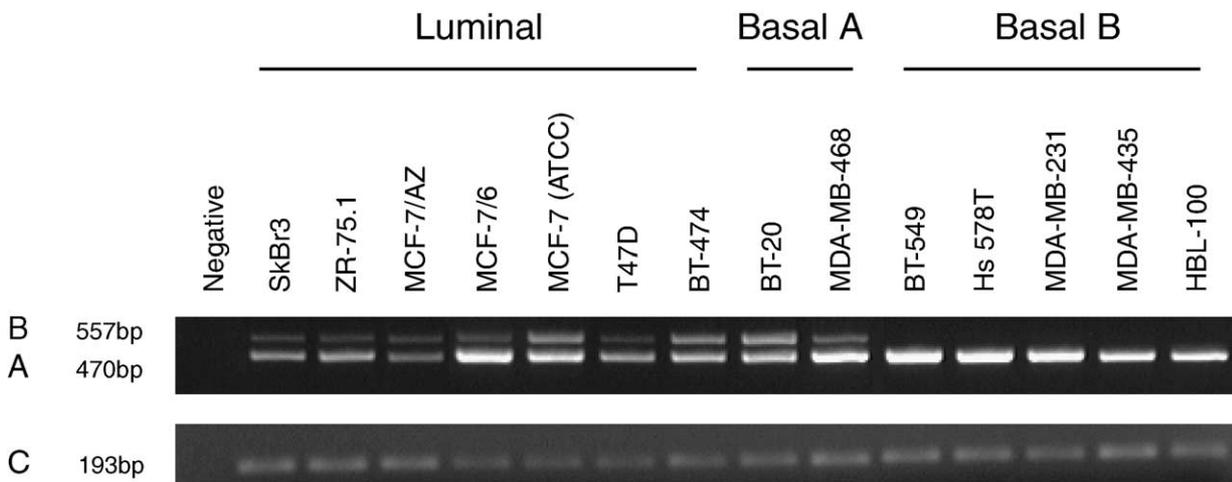


Fig. 4. mRNA expression of p120ctn isoforms generated by the alternative use of exons 20 (B), 18 (A) and 11 (C), in breast cancer cell lines. Numeric isoform codes and their sizes are indicated on the left.

scribed in all the cell lines studied, although at a very low level. Moreover, exon A was transcribed by all the cell lines we studied, whereas exon B was spliced out in the Basal B group, probably implicating functional differences at the biological level.

Additionally, we correlated p120ctn isoform expression profile with E-, P- and N-cadherin expression of different cell lines. We observed that transcripts of longer isoforms, such as 1.2, 1.3 and 2.1, were observed in N-cadherin positive cell lines, but also in MDA-MB-468 cells which expressed both E- and P-cadherin but not N-cadherin. Similarly, we found 2.2 and 2.3 variants either in E- and P-cadherin positive cell lines (T47D, BT-474 and BT-20) or in those expressing N-cadherin. Furthermore, SkBr3 cells, which were negative for all the analysed cadherins, exhibited a p120ctn isoform transcription profile similar to those lines displaying only E-cadherin or E- and P-cadherin together (except MDA-MB-468). These results suggest the possibility that the recruitment of p120ctn isoforms may be not directly related with the expression of a certain cadherin.

### 3.3. Protein expression of E-, P- and N-cadherin and p120ctn isoforms in breast cancer cell lines

To further evaluate the protein expression of cadherins and different p120ctn isoforms, we performed

an immunoblotting analysis using cell lysates of the whole breast cancer cell lines collection (Fig. 5). In general, cadherin protein expression levels were consistent with RT-PCR results. Relatively to p120ctn protein expression, several bands were also recognized in the immunoblot, which we interpreted like follows, based on previous knowledge: two faster migrating bands, with a molecular weight around 90 kDa, corresponding to type 3 isoforms (including variants 3.1–3.4); a single 100 kDa band combining three distinct p120ctn variants (1.3, 2.2 and 2.3); and two slower migrating bands, with approximately 120 kDa, representing 2.1 and 1.2 variants. Consistent with mRNA expression results, type 3 isoforms were expressed by all the cell lines, whereas the heaviest variant 1.1 was not found in anyone. In contrast, 2.1 variant, which could rarely be detected in the majority of Luminal cell lines by RT-PCR analysis, was generally present in the whole collection (except in MCF-7/6 cells). Variant 1.2 was typically expressed by Basal B cell lines and did not appear in Luminal cells. Additionally, this long p120ctn isoform was observed in either N-cadherin positive cells or in MDA-MB-468, which expressed both E- and P-cadherin, but not N-cadherin. Once more, these results confirm that the expression of p120ctn isoforms in breast cancer cells is associated with genomic and molecular features presented by each cell line, and possibly independent of the expressed cadherin.

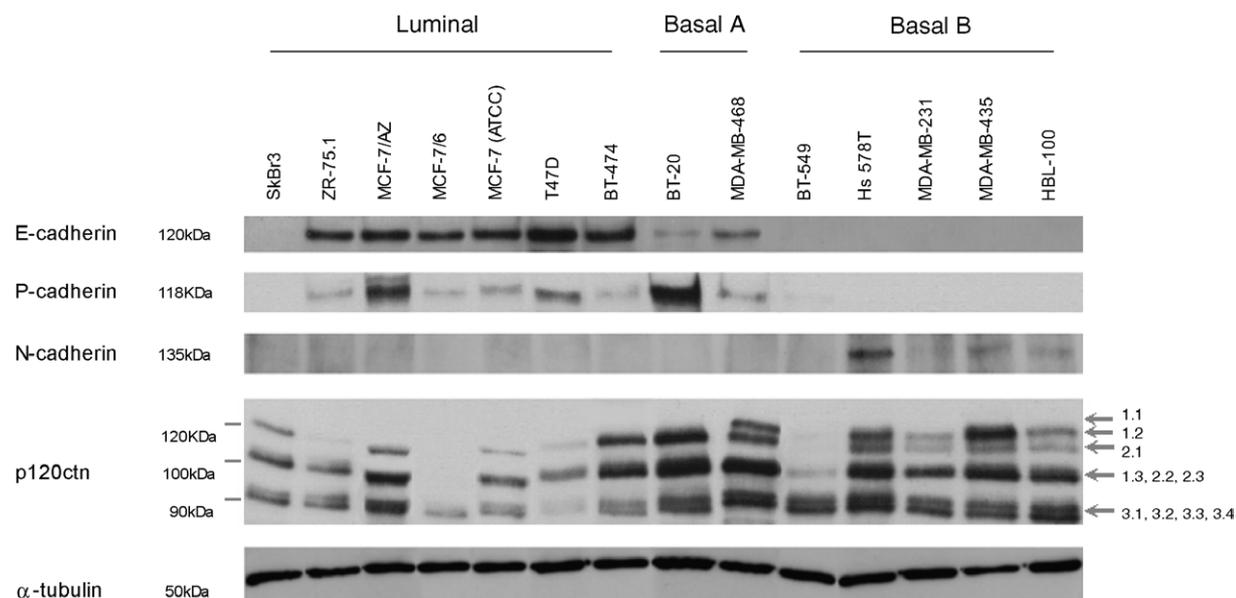


Fig. 5. Differential E-, P- and N-cadherin and p120ctn protein expression among breast cancer cell lines, analysed by Western blotting. Molecular weights are indicated on the left, while numeric p120ctn isoform codes are represented on the right. Immunostaining for anti- $\alpha$ -tubulin was done to control for equal loading.

#### 4. Discussion

The ability of p120ctn to generate multiple isoforms from a single gene constitutes a distinctive property that has deserved researchers' attention. Particularly in this study, we investigated the expression of these splice forms in a panel of breast cancer cell lines with distinct genomic and transcriptional properties. The results show that the recruitment of a p120ctn isoform in mammary cancer cells is cell-type-specific, depending from specific cellular genomic and transcriptional properties. In fact, we observed that each transcriptionally defined subgroup of breast cancer cell lines had a characteristic p120ctn isoform expression profile: Luminal cells mainly expressed type 2 and 3 isoforms and did not display the long 1.2 splice form; Basal B cell lines typically expressed 1.2 variant, but also displayed type 2 and 3 isoforms; Basal A cells, which exhibited either Luminal-like or Basal B-like genomic and biological features, showed one of the p120ctn isoform expression patterns of either of those subgroups.

Since the different transcriptional profiles described by Neve et al. to breast cancer cell lines were clearly correlated with distinct cellular morphology and behaviour [29], p120ctn isoforms may also be associated with particular biological characteristics. Therefore, 1.2 variant, typically exhibited by Basal B group, may be associated with lower cell differentiation and highly invasive capacity. In contrast, type 3 isoforms, predominantly expressed in Luminal cell lines, are probably implicated in the maintenance of tight intercellular junctions, higher cell differentiation and lower invasive capacity. This confirms previously reported data indicating that type 1 isoforms played a key role in the acquisition of a more cell invasive behaviour [26], whereas shorter isoforms were characteristically expressed by adhesive and less invasive cells [27]. Basal A cells might have either Luminal-like or Basal B-like morphologies, justifying again their variable p120ctn isoform expression pattern.

The existence of cell-type-specific expression patterns in breast cancer cells probably implicates functional differences between p120ctn isoforms. Little is known about the biological role of these different isoforms, but it was previously reported that specific sequences determine the subcellular distribution and functional significance of each isoform. In fact, a nuclear localization signal (NLS) was identified between the Arm repeats 6 and 7, and was implicated in directing p120ctn isoform 1 to the nucleus [32]. A second NLS, located immediately upstream from the Arm

domain, was also recognized as an inducer of type 2 and 3 isoforms nuclear localization. Although this nuclear accumulation of p120ctn appears coincident with the development of a cell branching phenotype, which is characterized by the presence of long dendritic-like processes [33], it is not clear whether the nuclear trafficking of this catenin is a cause or a consequence of this cellular phenotype [32]. On the other hand, two nuclear export signals (NESs) can efficiently mediate p120ctn expression from the nucleus (one found only in isoforms encoding exon B [22], other in the Arm repeat 8 of multiple splice forms [34]) suggesting that different isoforms could use distinct pathways for nucleocytoplasmic trafficking. Interestingly, we observed that exon B is differentially expressed among the collection, being absent in Basal B cell lines, which appeared lesser adhesive and highly invasive. This differential expression could be related to regulation of the transcription factor Kaiso and modulation of Wnt/ $\beta$ ctn signalling pathway. Perhaps, p120ctn isoforms lacking exon B can easily accumulate in the nucleus, where they can inhibit Kaiso's transcriptional repression of its target genes, possibly including those directly involved in proliferation and motility of cancer cells. Furthermore, the existence of specific phosphorylation sites in p120ctn may also contribute for functional differences among isoforms. Particularly, tyrosine residue 96 was only identified in type 1 splice forms, suggesting a potential role in cell motility [35]. Once p120ctn phosphorylation status seems to be critical in the regulation of cadherin-mediated adhesion, further research is required to clarify its effective contribution for cellular behaviour, under different conditions or in specific cell types.

It has been widely reported that cadherin switch plays an important role in cancer progression. Specifically, cells undergo a transition from an epithelial to a more mesenchymal phenotype (epithelial to mesenchymal transition – EMT), characterized by the loss of E-cadherin expression and increased expression of mesenchymal cadherins, such as N-cadherin, cadherin-11 or R-cadherin [36]. An identical p120ctn isoform switch during EMT has been proposed, although this is still a matter of debate. Some groups described an up-regulation of type 1 isoforms and down-regulation of type 3 variants in human epithelial cancer cells, in response to EMT-inducing transcriptional repressors [37,38]. However, other researchers did not see a consistent p120ctn isoform switch in cells expressing R-cadherin [17]. Additionally, it was suggested that longer p120ctn isoforms were preferen-

tially associated with N-cadherin, whereas shorter type 3 splice forms were linked to E-cadherin [27]. Similarly, Sarrió et al. proposed that E-cadherin-negative breast cancer cell lines were associated with isoforms type 1 and 3, whereas E-cadherin-positive cells did not express type 1 isoforms [37]. In this study, we evaluated the expression of p120ctn isoforms in a panel of breast cancer cell lines expressing different cadherins, and we did not observe an isoform preference for a particular cadherin type. Indeed, the majority of E- and P-cadherin-positive lines exhibited a p120ctn isoform expression profile similar to SkBr3 cells (negative for the three studied cadherins); likewise, MDA-MB-468 cells (expressing both E- and P-cadherin) displayed the same p120ctn isoforms as N-cadherin-positive cell lines. However, further studies are required to clarify if the recruitment of p120ctn isoforms is not strictly associated with the expression of a particular cadherin type.

In summary, our study is the first demonstrating that mammary tumour cells exhibit a characteristic p120ctn isoform expression profile, depending on their genomic and transcriptional properties. These particular expression patterns, combined with other regulatory proteins and in a specific cellular context, could explain how p120ctn could either contribute to strength intercellular adhesions or promote cell motility.

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### Competing interests

The authors declare that they have no competing commercial interests in relation to the submitted work.

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