# Notch-1, CD44v6 and N-cadherin expression profiles in colorectal cancer: Implications in precision medicine.

Vassilis G. Giannakoulis[1] , Agapi Kataki[1] , Anastasia Derventzi[1] , Konstantinos Papiris[2] , Eythimios Koniaris[3] , George Zografos[1] , Manousos Konstadoulakis[4]

[1] 1st Department of Propaedutic Surgery, Hippokrateio, Hospital, Athens Medical School, NKUA
[2] Department of Endoscopy, Hippocration General Hospital of Athens, Athens, Greece
[3] Department of Pathology-Anatomy, Hippocration General Hospital of Athens,
[4] 2nd Surgery Clinic, Aretaieio Hospital, Athens Medical School, NKUA

**Introduction:** Recent findings indicate Notch-1, CD44v6 and N-Cadherin as crucial factors in colorectal cancer (CRC) progression and although Notch-1 seems to have a leading role, their interplay during disease's evolution has not yet been elucidated. The present study attempts to explore their role in CRC progression, in order to enrich the number of biomarkers available for CRC patients' stratification into subgroups and allow a more efficient personalization of therapies in the future.
**Methods:** Notch-1 and CD44v6 expression were determined by flow cytometry analysis in frozen tissue samples from 34 CRC patients (11 females and 23 males; mean age 71.71 years; range 53-87; 10,10,12,2 patients in stages I,II,III,IV respectively) and 8 colorectal polyps (5 females and 3 males; mean age 63.83; range 49-79). Tissue N-cadherin expression was determined by RT-PCR. Protein expression profiles were evaluated statistically for their correlation with patient demographic and clinicopathological variables (primary tumor sidedness, stage, grade, and lymph node metastasis).
**Results:** Notch-1 protein expression was significantly higher in CRC tissues compared to colorectal polyps (77.76% ±1.79% vs 56.75% ±7.09%, p= 0,005). No statistical significance differences were observed between the different stages or grades of CRC patients. CD44v6 expression although increased in cancer lesions failed to reach a statistical significance (24.85% ±1.69% vs 19.39% ± 5.04%, p=0.051). Still, Spearman's Rho Calculator showed a strong positive correlation between Notch-1 and CD44v6 expression (R=+0.647, p<0.001). Notch-1 expression was found increased among the 23 CRCs lesions detected positive for NCadherin mRNA expression (80% ± 2.13% vs 73% ± 2.94%, p=0.014). N-cadherin expression was more prominent in stage II-IV CRC lesions (79.2% vs 40%, p=0.045). Induced CD44v6 was detected in right-sided CRC lesions compared to left-sided (31.45% ± 2.84% vs 22.1% ± 1.84%, p=0.008) or colorectal polyps (31.45% ± 2.84% vs 19.39% ± 5%, p=0.013).
**Discussion:** Presented data provide further evidence that Notch-1 expression is a key element in CRC development, most probably from the early phases of the disease, as its expression was not related to stage or grade while, its co-expression with N-cadherin supports its involvement in the Epithelial-to-Mesenchymal transition of cancer cells. Also, the observed association between N-cadherin positive tissues and cancer stages indicates N-cadherin's involvement in advanced CRC stages. Additionally, CD44v6 expression profile was supportive of the concept that proximal and distal CRCs are distinct clinicopathologic entities.
**Conclusion:** The feature that Notch-1 plays a central part in CRC progression from disease's early stages, identifies it as a target to exploit in Notch-based therapeutics. Furthermore, Ncadherin targeted therapies may be more appropriate in advanced stages. Finally, anti-CD44v6 therapy should be considered as a candidate for the therapeutic approach of proximal colon cancers.

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