

# Presenter Disclosure Information

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The following relationships exist  
related to this presentation:

No Relationships to Disclose

Identification of colon cancer  
associated antigens:  
key therapeutic targets  
in the prevention of  
disease relapse or progression

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# Introduction

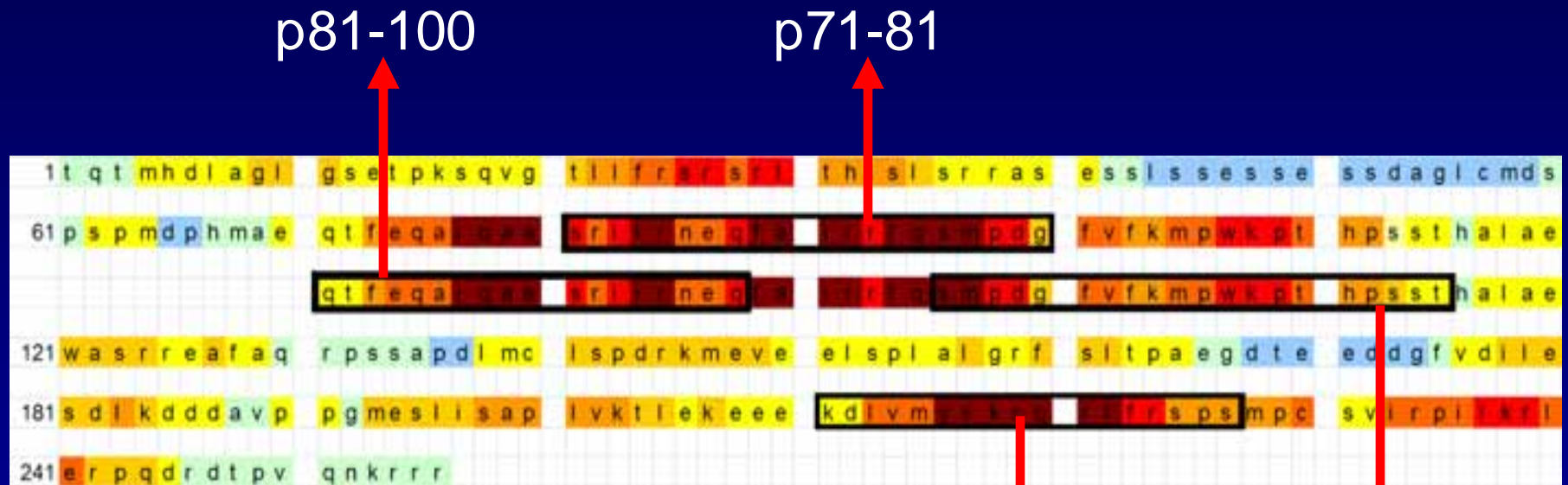
- Colorectal cancer (CRC) is the second leading cancer in the US
  - 146,000 new cases and 50,000 deaths
- Adaptive immune response may play role in preventing tumor recurrence
- Vaccine could boost cellular immunity
- Few defined immunogenic proteins
- Can we identify antigens suitable for a CRC vaccine?

# Methods

- Systematic literature search using key words, i.e. colon cancer, prognosis, multivariate analysis
  - 125 papers identified
- 8 proteins evaluated based on:
  - Incidence of expression
  - Independent predictor of poor prognosis
  - Independent predictor of early disease recurrence
  - Known biologic function
- Algorithm to identify peptides predicted to be high affinity binders across multiple HLA DR alleles

| <b>Protein</b>   | <b>Function</b>   |
|------------------|---|
| CDC25B           | cell cycle overexpression   |
| COX-2            | cell proliferation, inflammation  |
| EBAG9/<br>RCAS1  | inhibits cell growth/ apoptosis of T,B, NK cells                                      |
| EGFR*            | cell division, migration, angiogenesis  |
| FASCIN           | cell-cell interaction and adhesion, actin-based structures, cell locomotion           |
| IGF1R*           | enhances cell survival, anti-apoptotic agent  |
| PRL-3/<br>PTP4A3 | cancer cell migration and proliferation, angiogenesis, invasion and metastasis        |
| VCP              | anti-apoptotic function and metastasis via activation of NF-kappa B signaling pathway |

# CDC25B phosphatase heat map



Predicted binding x # DR alleles

Top quartile: Orange-red-brown

Mid quartiles: Yellow-gold

Bottom quartile: Blue-green

p111-128

p96-115

# Predicted “hot spot” density varies

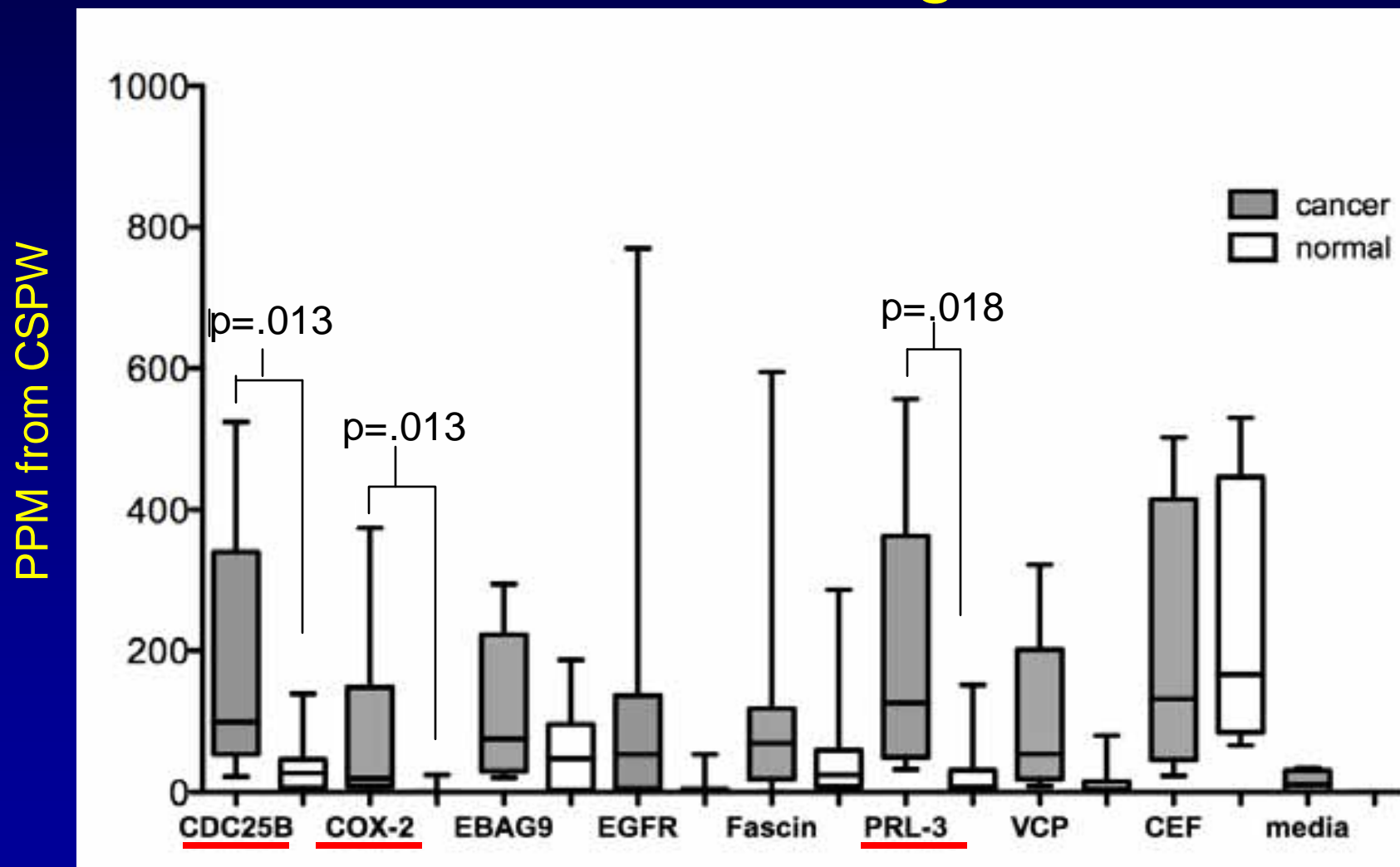
**PRL-3: p12-30, p33-53, p104-122, p124-142**



**VCP: p49-65, p82-102, p138-156, p161-180**



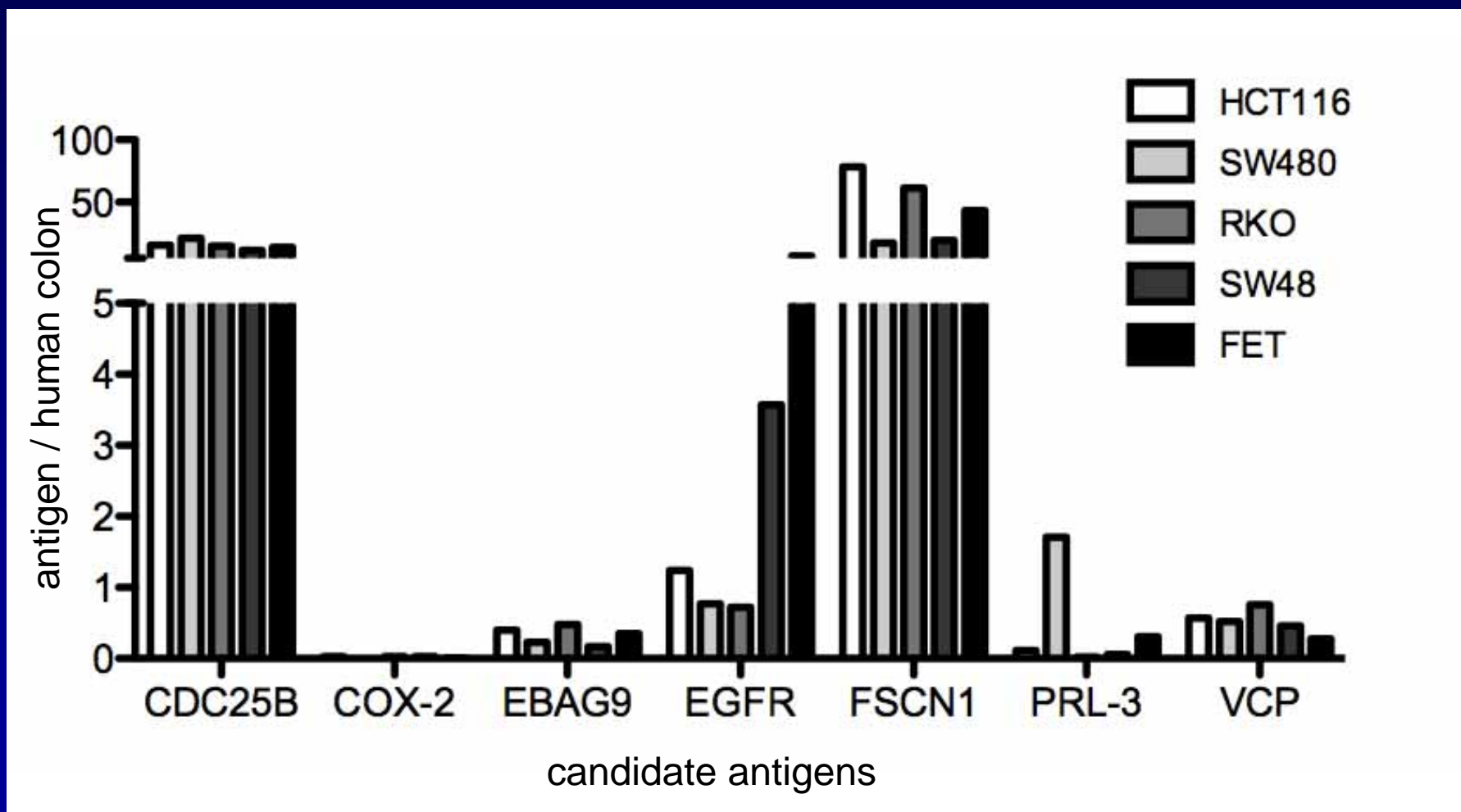
# IFN- $\gamma$ ELISPOT response to candidate antigens



(n=10)

candidate antigens

# Gene expression of candidate antigens in CRC cell lines



MSI (HCT 116), CIMP (RKO, SW48), CIN (FET, SW480)

# Conclusions

- Biologically relevant CRC associated proteins can be identified:
  - Associated with prognosis
  - Potentially overexpressed in majority of CRC
- Epitopes predicted to bind multiple DR, derived from candidate antigens, elicit T cell responses in CRC patients > controls
- Candidate antigen gene expression across different CRC phenotypes
- These antigens may represent novel immunologic targets for CRC

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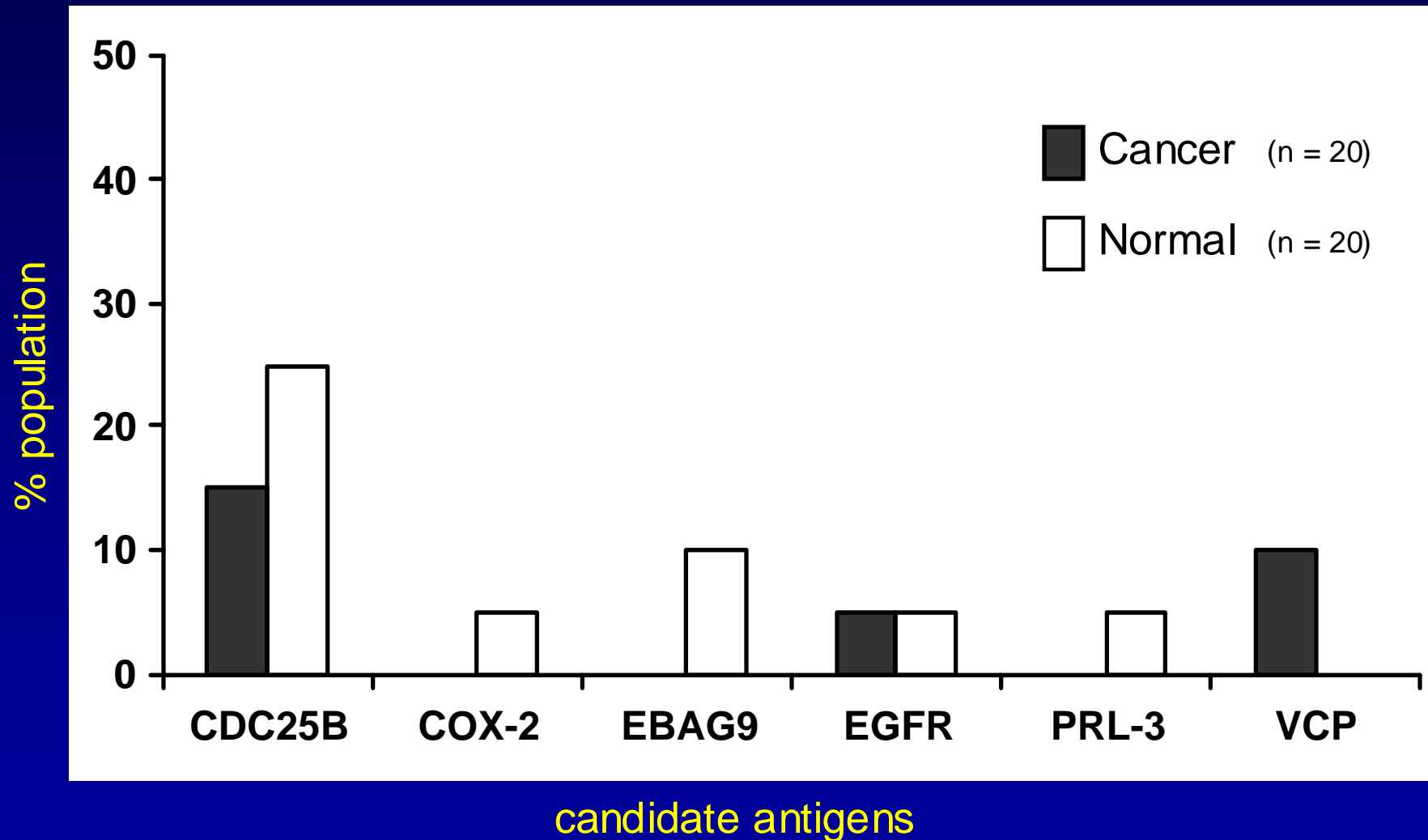


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# Candidate antigen specific IgG antibody response



Positive: Mean + 2 SD of controls