**TRANSCRIPTION FACTORS AND IMMUNE CHECKPOINT MOLECULES**

**INTRODUCTION**

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Immunosenescence = Decline in the function of the immune system with increasing age

Cancers and chronic diseases were significantly increased after 50 yrs

With increasing age, the abnormal altered DNA was significantly increased

Tumor suppressor genes slow down cell division, repair DNA mistake and lead cells to apoptosis (programmed cell death)

NEW CANDIDATES OF TUMOR SUPPRESSOR GENE IN AGING?
**WHAT DO WE KNOW ABOUT BACH2?**

BACH2 repression in CD4+ T cells modulates their resistance to apoptosis demonstrating its function as a Tumor Suppressor Gene

BACH2 is highly sensitive to DNA damage and Aging (mice)

BACH2 mediates immune homeostasis by suppressing PRDM1 in both T cells and B cells to (mice)

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**UPREGULATION of INHIBITORY IMMUNE CHECKPOINT, PD-1 and PD-L1**

Cancer cells can express PD-L1 and by interacting with PD-1 on T-cells, they can inactivate and block the anti-tumor immune response

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**PREDICTIVE MARKERS OF IMMUNOSENESCENCE?**

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**METHODS**

**Population:** Peripheral blood samples were obtained from 60 healthy donors (HDs) between the ages of 20 to 90 yrs and 40 untreated patients with chronic lymphocytic leukemia (CLL).

**Statistical analyses:**
- Mann-Whitney test (p) was used to compare the distribution of two unmatched groups.
- Spearman’s correlation (r) was used to measure the correlation between sets of data.

**Phenotype analysis by flow-cytometry:**
- Freshly purified PBMC.
- Common markers for major lymphocyte subsets (CD45, CD3, CD4, CD8, CD19…).

**Lymphocyte subsets purification:**
- MACS magnetic isolation of CD3+CD4+; CD3+CD8+ and CD19+ subsets (the purity between 95%-99%).

**Real-time quantitative RT-qPCR:**
- BACH2 and PRDM1 mRNA transcripts were quantified in the purified lymphocyte subsets.

**Western Blotting:**
- BACH2 and BLIMP1 (PRDM1) protein expression in the purified lymphocyte subsets.
The number and activity of CD8+ T cells and the number of Naïve cells decrease by age

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<thead>
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<th>Young (≤50)</th>
<th>Old (&gt;50)</th>
<th>P value</th>
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<tbody>
<tr>
<td>CD8+ T cells/μl</td>
<td>3000</td>
<td>2000</td>
<td>0.002</td>
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<tr>
<td>Naïve cells/μl</td>
<td>400</td>
<td>500</td>
<td>0.009</td>
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**BACH2** and **PRDM1** gene expression were strongly correlated with age in major lymphocyte subsets from healthy donors.

**PD-1** and **PD-L1** gene expression were correlated with age in major lymphocyte subsets from healthy donors.

**BACH2**, **PRDM1**, **PD-1** and **PD-L1** were even more pronounced in T cells and leukemic B cells from CLL patients.

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BACH2 protein expression was decreased in older healthy group and CLL patients

PD-1 and PD-L1 protein were highly expressed in T cells and leukemic B cells from CLL patients

CONCLUSION

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Our observations data suggest that:

- PD-1/PD-L1 expression is upregulated according to age
- Transcription factor BACH2 and PRDM1, in inverse correlation, are strongly correlated with aging
- Those effects are even more pronounced in T cells and leukemic B cells from chronic lymphocytic leukemia patients

BACH2, PRDM1, PD-1 and PD-L1 genes could be PREDICTIVE MARKERS of IMMUNOSENESCENCE

ACKNOWLEDGEMENTS:
Prof. Dominique BRON
Dr. Catherine SIBILLE
Dr. Karen WILLARD-GALLO
Hematology Department
Hematology Laboratory
Molecular Immunology Unit
Jules Bordet Institute, Brussels, Belgium
Yvonne Boel Foundation, Brussels, Belgium