Do immunological events play a role in chordoma?

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Differential lymphocyte infiltration in chordoma
Frequency of lymphocyte infiltration in chordoma tumors

- Patients: # 62
- Blocks examined: #387
- Lymphocyte-positive: #52
- Lymphocyte-negative: #10

- Lymphocyte-negative, N = 125
- Lymphocyte-positive, N = 262
Tumor microenvironment and lymphocyte infiltration

Does the lymphocyte infiltration reflect

i) a patient’s immune response against his own tumor or

ii) a non specific inflammatory response?

Besides contributing to the understanding of the role of immunological events in the pathogenesis of chordoma, the answer to these questions has important prognostic and therapeutic implications.
Role of immunosurveillance in malignant cell elimination

Normal cell → Tumor cell

Elimination of tumor cells by lymphocytes
Escape of tumor cells from immunosurveillance

Loss of molecules crucial for malignant cell recognition by host immune system
Development of HLA class I negative tumors

A CTL response eliminates + cells

Survival of - cells

Predominance of - cells
MHC class I antigen processing machinery
Differential HLA molecules expression in chordoma

positive

negative

HLA-class I

HLA-class II
Differential β2-microglobulin expression in chordoma
Differential HLA antigen processing machinery components expression in chordoma

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<thead>
<tr>
<th>positive</th>
<th>negative</th>
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<tr>
<td><img src="image1" alt="TAP1 positive" /></td>
<td><img src="image2" alt="TAP1 negative" /></td>
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<td><img src="image3" alt="Tapasin positive" /></td>
<td><img src="image4" alt="Tapasin negative" /></td>
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<td><img src="image5" alt="Calreticulin positive" /></td>
<td><img src="image6" alt="Calreticulin negative" /></td>
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Conclusions

i) Lymphocyte infiltrates are present in chordoma tumors

ii) Defects in HLA antigen expression in chordoma tumors suggest that lymphocyte infiltrates reflect a patient’s immune response to his own tumor
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Questions to be addressed

i) What is the nature of the tumor infiltrating lymphocytes?

ii) Do they reflect the development of a tumor antigen specific immune response?

iii) Which tumor antigen are recognized by the patients immune system?
Questions to be addressed

i) Can the patients immune response be enhanced by appropriate immunization strategies?

ii) Can antibodies targeting inhibitory molecule improve the ability of the patient immune system to eliminate malignant cells?
Questions to be addressed

i) What are the molecular mechanisms underlying the defects in the expression of HLA Class I antigen processing machinery components?

ii) Do these defects play a role in the clinical course of the disease?

iii) Can these defects be corrected by immunomodulatory agents?