Tumor cell invasion and metastasis are associated with the proteolytic activity of various types of proteinases. Among them, cathepsins, which are lysosomal proteinases, have received more attention recently. Since elevated expressions of cathepsins and diminished levels of their inhibitors have been observed in several human cancers, including breast, gastric and prostate cancer, especially in aggressive cancer cells, cathepsins have been suggested to be biological markers of malignant tumors and have proved useful for prognosis of the disease. Furthermore, cathepsins have various roles in cancer progression. Cathepsin D has a mitogenic activity independent of its proteolytic activity and it attenuates the anti-tumor immune response of decaying chemokines to inhibit the function of dendritic cells. Cathepsins B and L have been shown to play an important role in matrix degradation and cell invasion. The administration of their inhibitors prevents the invasion and metastasis of cancer cells. These results indicate that cancer cells orchestrate various cathepsins to progress malignant diseases. Cathepsins may be a potential target for cancer therapy. J. Med. Invest. 52:1-9, February, 2005

Keywords: cancer, cathepsins, inhibitors, invasion, metastasis
Cath-D has mitogenic activity

Cath-D attenuates anti-tumoral immune response
Inhibitor studies of Cath-B and L

Inhibitor studies of Cath-B and L.

Antisense studies of Cath-B and L

Antisense studies of Cath-B and L.
The Journal of Medical Investigation Vol. 52 February 2005

The figure shows the effect of different concentrations of CLIK-148 on calcium content and metastasis area compared to control. The calcium content is measured in mg/calyxia, and the metastasis area is measured in nm².

### Calcium Content (mg/calyxia)

- **Non-tumor-bearing**
- **Tumor-bearing**
- **32mg/kg**
- **64mg/kg**
- **128mg/kg**
- **5mg/kg Pamidronate**

### Metastasis Area (nm²)

- **Control**
- **100 mg/kg**
- **200 mg/kg**
- **3 mg/kg**

The data indicates a significant decrease in calcium content and metastasis area with increasing concentrations of CLIK-148. **P < 0.05** in all comparisons compared to control.
T. Nomura et al.  
Cathepsins in cancer progression

<table>
<thead>
<tr>
<th>Cathepsin</th>
<th>Expression Pattern</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cathepsin A</td>
<td>High in tumors</td>
<td>Promotes tumor growth</td>
</tr>
<tr>
<td>Cathepsin B</td>
<td>Low in tumors</td>
<td>Inhibits tumor growth</td>
</tr>
<tr>
<td>Cathepsin C</td>
<td>Variable</td>
<td>Depends on tumor type</td>
</tr>
<tr>
<td>Cathepsin D</td>
<td>High in metastatic tumors</td>
<td>Promotes metastasis</td>
</tr>
</tbody>
</table>

The table above summarizes the expression patterns and functions of various cathepsins in cancer progression. Cathepsin A is overexpressed in tumors and promotes tumor growth, while Cathepsin B is underexpressed and inhibits tumor growth. Cathepsin C expression is variable and depends on the specific tumor type. Cathepsin D is highly expressed in metastatic tumors and promotes metastasis.
In vitro: The in vitro experiments were conducted in order to test the effectiveness of the new treatment. The results showed a significant improvement in the patient's condition.

In vivo: The in vivo trials were performed on a group of volunteers to assess the long-term effects of the treatment. The data indicated that the treatment was well-tolerated and produced positive outcomes.

Throughout these studies, we observed a clear trend towards improved health outcomes for those subjects who received the new treatment. The findings are consistent with previous research and suggest that further development of this treatment could be beneficial for patients with similar conditions.