P1-154 Mesothelioma and Other Thoracic Malignancy Posters, Mon, Sept 3

Antitumor effect of Telomerase-Selective Oncolytic Adenoviral Agent OBP-301 (Telomelysin) in pleural dissemination of human malignant mesothelioma

Kagawa, Shunsuke1 Watanabe, Yuichi2 Hashimoto, Yuuri2 Kojima, Toru1 Uno, Futoshi1 Kuroda, Shinji3 Urata, Yasuo1 Tanaka, Noriaki4 Fujisawa, Toshiyoshi1

1 Center for Gene and Cell Therapy, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan 2 Okayama University Graduate School of medicine, Okayama, Japan 3 Oncolys BioPharma, Inc., Okayama, Japan 4 Oncolys BioPharma, Inc., Tokyo, Japan

Background: Malignant mesothelioma is an extraordinarily challenging disease to treat; however, locoregional virotherapy may be applicable for this aggressive disease because of the accessibility by intrapleural and/or intratumoral virus delivery. We previously reported that an attenuated adenovirus OBP-301 (Telomelysin), in which the human telomerase reverse transcriptase (hTERT) promoter element drives expression of E1A and E1B genes linked with an internal ribosome entry site, could replicate in and causes selective lysis of human cancer cells. In the present study, we examined the antitumor effect of Telomelysin on human malignant mesothelioma cell lines in vitro and in vivo.

Results: The XTT assay demonstrated that Telomelysin could efficiently kill four human mesothelioma cell lines H2052, H2452, H28, and 211H, all of which expressed the coxsackievirus and adenovirus receptor (CAR), in a dose-dependent manner. In vivo antitumor effect was also evaluated in an orthotopic pleural dissemination model. Intrathoracic administration of 2 x 10^8 plaque forming units (PFU) of Telomelysin markedly reduced the size (1 ± 1.8 mg vs. 190 ± 75 mg, p < 0.01) of H2452 tumors intrathoracically implanted into BALB/c nu/nu mice compared to mock-treated mice.

Conclusions: These results suggest that locoregional administration of Telomelysin into the thoracic cavity may be efficacious in the prevention and treatment of pleural dissemination of human malignant mesothelioma.

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Asbestos fiber concentration in lung tissue of patients with malignant pleural mesothelioma

Usami, Noriyasu1 Sakai, Kiyoshi2 Okasaka, Toshiki1 Ito, Shimon1 Uchiyama, Mika1 Yokoi, Kohei1

1 Division of Thoracic Surgery, Nagoya University Graduate School of Medicine, Nagoya, Japan 2 Nagoya City Public Health Research Institute, Nagoya, Japan

Background: Although the association between asbestos exposure and the development of malignant pleural mesothelioma (MPM) is well recognized, the relationship between asbestos contents by fiber type and the risk of development for MPM remains unclear. In this study, we evaluated the asbestos contents by fiber type in the lung and the primary tumor of patients with resected MPM.

Methods: Asbestos fiber contents in the pulmonary parenchyma and tumors were analyzed in 3 patients with MPM by transmission electron microscopy with energy-dispersive X-ray analysis using a low-temperature ashing procedure. The geometric mean content of total asbestos in the control subjects without history of asbestos exposure were used as reference, which was 1.83 x 10^6 fibers / g dry lung. (Reference: Sakai K et al. Asbestos Concentration and Fiber Size in Lungs of the Urban Residents. Japanese Journal of Public Health, 1991; 38: 762-770)

Results: Three patients were analyzed in this study, which were Case1: 50-year-old man, biphasic type, pT3N2M0 in the International Mesothelioma Interest Group staging system, Case2: 54-year-old man, biphasic type, pT2N0M0 and Case 3: 56-year-old man, epithelial type, pT4N0M0. All patients had a history of asbestos exposure and underwent an extrapleural pneumonectomy with curative intent. Asbestos fibers were not detected in the tumor tissues in all patients. The geometric mean content of total asbestos in lung tissues were 1.8 ± 1.4 (x 10^6 fibers / g dry lung), 54.2 ± 33.1 and 6.5 ± 3.7 in the case1, case2 and case3, respectively, which showed 1 time, 29.6 times and 3.6 times compared with that of the control subjects. The distributions of asbestos by fiber type in each patient were very different as following.

<table>
<thead>
<tr>
<th>Fiber Type</th>
<th>Case1</th>
<th>Case2</th>
<th>Case3</th>
</tr>
</thead>
<tbody>
<tr>
<td>chrysotile</td>
<td>71%</td>
<td>49%</td>
<td>11%</td>
</tr>
<tr>
<td>crocidolite</td>
<td>7%</td>
<td>42%</td>
<td>52%</td>
</tr>
<tr>
<td>amosite</td>
<td>7%</td>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>others</td>
<td>15%</td>
<td>2%</td>
<td>30%</td>
</tr>
</tbody>
</table>

Conclusions: Case1 had MPM without high level exposure of asbestos. On the other hand, case2 and case3 showed higher concentration of asbestos fiber in the lung tissue than control subject, which evidenced the high level exposure of asbestos. Those two patients also had a large proportion of crocidolite in the total asbestos fibers, which might be associated with the development of MPM. To elucidate the relation between the pulmonary asbestos fiber contents by fiber type and development of MPM, further investigation is considered necessary.

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Endobronchial metastasis of tumors of other primary origin

Uskokovic-Stefanovic, Zivka; Bukurov-Sudjic, Emilija; Popevic, Spasoje

Institute for Lung Diseases and TB, Belgrade, Serbia

Lungs represent one of the most common sites of secondary deposits of various primary tumors. However, incidence of endoluminal metastases is low(2-28%)because fiberoptic bronchoscopy is not performed routinely in all patients(pts) with pulmonary metastases. Also,these patients may also have low performance status and diagnosis is provided by other procedures.

During 2005 in our department 3724 bronchoscopies were done,mostly under suspicion on lung cancer.In 46(1.23%)endobronchial metastases were found.