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Survival signal pathways as potential therapeutic targets in soft tissue and osteo sarcoma cell lines

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Introduction Soft tissue sarcomas (STS) are rare malignancies but have poor survival rate. The investigations for targeted therapy are underway but little is known about potential targets until now. We previously presented potential molecular targets in osteosarcoma (OS) cell lines (101st AACR annual meeting 2010, abstract No.2451). We tried to compare the protein and mRNA profilings between the OS and STS cell lines to suggest the feasibility for developing molecular targeted agents in STS. Methods We examined the protein expression of c-Met, Akt, mTOR, and their phosphorylated status, and PTEN in seven OS (MG-63, HOS, KHOS/NP, SK-ES-1, U-2OS, Saos-2, and G-292) and five STS cell lines (SK-UT-1, A-673, SW-871, SW-982, HT-1080) using western blotting. The gene expression profilings of the cell lines were performed by 44K microarray (Agilent Inc.). Results Microarray data showed that whole genome expression pattern of STS was different from OS cell lines. But, the expressions of 94 mRNAs within the signal transduction pathways, which represent the currently utilized drug targets, revealed similar pattern between two groups of cell lines. To verify the possibility of developing molecular targeted agents in STS, we examined the activation patterns of signal transduction pathway proteins in each STS cell line. All STS cell lines except A-673 with low c-Met, but high p-Met, expressed moderate level of c-Met and p-Met. PI3K was expressed in all cell lines, with higher p-PI3K in SK-UT-1 and A-673 than in other STS cell lines. All but SW-872 cell line expressed Akt, and SK-UT-1, SW-872 and HT-1080 had higher levels of p-Akt. SW872 showed negligible PTEN and high level of p-Akt. SW982 generally repressed level of p-Met, p-PI3K, p-Akt, p-mTOR comparing with other STS cell lines. Meanwhile, mTOR and p-mTOR were expressed relatively even in all STS cell lines. Conclusion We presented that STS cell lines had variously activated signal pathway status as in OS cell lines. Common potential targets such as mTOR was revealed, and the specific targets including PI3K or Akt were also presented. It suggests the possibility of developing specific molecular targeted agents in each type of STSs.

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Chemotherapy response related massive bleeding and management

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The goals of palliative chemotherapy are to improve overall survival and the quality of life through relief of symptoms. The other hand, chemotherapy has many side effects such as myelosupression, neuropathy, gastro-intestinal symptom and infertility. In many known side effects of chemotherapy, bleeding occurs in approximately 6-10% of patients with advanced cancer. Most of bleeding is local vessel damage and systemic process such as disseminatated intravascular coagulopathy, abnormalities in platelet function or number after chemotherapy. There is no article about chemotherapy response related bleeding. However, bleeding may occur in chemo-sensitive tumor like lymphoma and in pre-radiotherapy patient such as head and neck cancer, rectal cancer after chemotherapy. There are three cases of pure chemotherapy response related bleeding without other bleeding condition. One is pre-radiotherapy given maxillary sinus cancer, another is chemo sensitive gastric cancer and the last case is pre-radiotherapy given rectal cancer. These all cases had a massive bleeding after chemotherapy without other bleeding condition and successful management variable method such as embolization, endoscopy, and thrombotic agent.