

Research and Development of *Wedelia chinensis* to Treat Cancer Progression and Metastasis

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Signaling pathway of androgen receptor plays a central role in the prostate cancer progression. Accordingly, approaches and molecular mechanisms to ablate the androgen receptor function in prostate cancer have been actively studied to improve the disease treatment. However, the disease inevitably develops resistance to all forms of hormonal therapies. To further understand the clinical progression and metastatic development of prostate cancer, we established orthotopic xenograft model using various human cell lines expressing Luc2 reporter and/or fluorescence proteins by lentivirus-mediated infection. Growth of these orthotopic xenografts develops a wide spectrum of spontaneous metastases in vivo, from which we also obtained cells from more aggressive and metastasized tumors. Previously, we have identified that *Wedelia chinensis* contains three compounds synergistically inhibitory to the androgen receptor signaling and cell growth in malignant prostate cells. Focused on these principal active compounds, we have optimized the extraction procedure to offer standardized botanical preparations from *Wedelia chinensis*. Oral administration of the *Wedelia* extract to orthotopic xenograft models of human prostate cancer resulted in attenuation of the primary tumor growth and metastasis. Moreover, combination with hormonal therapy and docetaxel maximized the blockade of metastasis and resistance to chemotherapy of prostate cancer. The antimetastatic effect was also shown in other tumor models, suggesting a potential to prevent cancer metastatic development. Our study establishes in vivo development models of human prostate cancer and demonstrates the therapeutic efficacy of *Wedelia chinensis* in clinically relevant settings.