MATHEWS

Editorial

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Anti-Metastatic Drug Developments, Utility of More Animal Models

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ABSTRACT

Neoplasm metastasis is a multiple-step and multi-molecular pathogenesis process resisting to current norm of therapeutics. More seriously, there is a great shortage of effective and licensed anti-metastatic drugs worldwide. Several evaluative avenues of pharmaceutical efforts might change this scenario in the future. Preclinical tumor models *in vivo* are workable to embrace new therapeutic strategies and paradigms in the clinic. This Editorial provides latest views of advanced metastatic models *in vivo* and possible breakthroughs in drug evaluation and development.

Keywords: Neoplasm Metastases, Cancer Chemotherapy, Clinical Cancer Trial, Personalized Medicine, Animal Model, Brain Metastasis.

INTRODUCTION

Neoplasm metastasis is a multiple-step and high mortality feature of human malignant diseases (60-90% cancer mortality worldwide) [1-2]. Presently, chemotherapeutic efficacy against cancer metastasis was very low. Usually, therapeutic drugs are derived from *in vitro* tumor cell cultures of primary tumors in order to cope with large number of new compounds waiting for initial screening. Accordingly, antimetastatic drugs (several types available) are often used as assistant cancer therapy due to efficacy limitations [3-6].

Generally speaking, cancer patients' survival has been little changed whilst overt metastasis is observed [1-2]. Only drugs can be used against tumor metastasis. Therefore, any small breakthrough for drug developments can achieve unexpected therapeutic promotion and benefiting. This Editorial highlights biological and therapeutic novelty in this regard.

METHODS

Antimetastatic drugs have been reported over half a century [7]. The therapeutic targets and drug mechanisms are approximately ten categories. We outline them as several pathways; Tumor detachment, microenvironments, angiogenesis, tumor vascular circulation, cancer plasticity, cancer stem cells, immune regulators, glycol-conjugate inhibitors and others [3-6]; Despite numerous molecular pathways have

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been discovered to associate with neoplasm metastases [8-10], there is still greatly shortage of effective drugs for clinical metastasis trials. Several factors and causalities are proposed to affect the quality of drug development. As we can see, the evaluative quality in animal modalities plays critical roles to overcome many pathological or pharmacological obstacles.

Despite vast alley of newly synthetic or purified compounds needed for anticancer activity testing, drug evaluative architecture can affect the quality of drug screen and discovery. In the early stage of drug evaluation, tumor cell culture (*in vitro*) and tumor growth in mice (*in vivo*) played equal roles in drug screening.

More recently, drug evaluation *in vitro* plays dominant role in drug screening and mechanism studies. They are much quicker in drug evaluation and need much less human labor. Nonetheless, this kind of cell culture technique is deficiency for tumor metastatic evaluation. This might be the major reason and deficiency for the efficacies of anti-metastatic drug development.

DISCUSSION

The major difference between primary and metastasis tumors lies on tumor-host tissue interaction, drug activities and environmental adaptation. Only animal models can help us to understand metastatic pathogenesis pathways, network, drug efficacy and overall survival benefiting.

Technically, animal models for neoplasm metastasis increased in the past. In the beginning of drug screening in the National Institute of Cancer, the United States, only pulmonary metastatic models (melanoma B16 and Lewis lung carcinoma) were officially enlisted before clinical drug evaluation [11]. However, tumor metastasis is not only restricted in human lungs. Brain, bone, lymph-node and liver are also popular sites for metastatic colonization. In animal tumor models, blood-brain or other barriers may change drug delivery to metastatic sites. Now, tumor cells injected into spinal of mice were utilized for brain or bone metastatic treatment evaluations [12]. This is an important breakthrough for anti-metastatic drug screening.

FUTURE TRENDS

Besides the promotion of anticancer drug developments, cancer therapeutic study is also important route to improve cancer metastatic managements. Nowadays, there is a great advance in pharmaceutical delivery [13], drug resistance [14] and immunotherapeutic application [15] for metastatic treatment. Correspondingly, experiments in animal models are indispensable. It was proposed that primary tumors are inversely related with metastatic colony in drug efficacy and inhibition [16]. It is very suitable for in vivo anti-metastatic treatment studies by animal modalities, especially in mice.

In these items of clinical cancer therapeutic options, drug combinations, herbal medicine and personalized medicine deserve further elucidation [17-21].

CONCLUSION

To conclude, we shall evaluate much more agent's benefiting by animal models from injecting different tumor subtypes into murine spine (brain or bone metastasis) and blood vessels (liver or lung metastasis) in the future. The hope for this kind of evaluative network may pave the way for more therapeutic paradigms and success sooner or later.

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