

Eradication of Tumor Cells and the Serious Impact of Adverse Effects

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EDITORIAL

The objective in formulating a SFM is to supplement a basal medium such as DMEM/F12 with essential components such as growth factors, vitamins, trace elements, hormones and any other micronutrients not provided by the basal media. Early attempts to develop SFM formulations incorporated such animal-sourced components as insulin, transferrin, albumin and cholesterol. However, these first-generation formulations still had the disadvantages of containing relatively high protein content and components that were derived from animal sources. There followed two important, but separate, criteria for SFM: protein-free (PF) and animal-derived component-free (ADCF). ADCF media may contain recombinant proteins and protein hydrolysates derived from non-animal sources. For PF media, proteins may be replaced by low-molecular-weight components including peptides, hormones and inorganic salts. However, in many cases commercially available media described as PF contain minimal levels of recombinant proteins. As a young scientist, I was interested in antibody-drug conjugates (ADCs) because of my background in immunochemistry and previous experience in the development of antibody derivatives. The idea was based on a concept originally advanced by Paul Ehrlich, to create a magic bullet for cancer treatment, long before such tools became available. Many different toxic substances were available as the payload, most of which had already been used in chemotherapy, albeit with the risk of serious adverse effects due to their nonspecific activity. Batch-to-batch variation in composition: the composition of serum is variable and unde-fined, which leads to inconsistent growth and productivity. Each batch can vary in content depending upon the diet and condition of the donor cows. This variation can cause significant differences in the growth-promoting characteristics, and ultimately causes significant differences in productivity of the cell-culture process. I was asked to participate in a project involving the conjugation of cytotoxic drugs to monoclonal antibodies that

specifically recognized tumor-associated antigens. Chemotherapy needed to be aggressive and oncologists managed a fine line between the quantitative eradication of tumor cells and the serious impact of adverse effects. The study was financed by the European Community under the framework program Europe Against Cancer and its mission was clear. Little had changed 16 years after the signing of the National Cancer Act (1971), which US President Richard Nixon often referred to as “the war on cancer”, despite dramatic improvements in certain areas of cancer therapy. In the meantime, however, basic research had helped to create a better understanding of cancer biology, improved diagnostics and tumor-associated surface proteins that were thought to be ‘undruggable’ came under scrutiny for targeted therapies. The chemical identity of all the bioactive components needed for cell growth leading to a fully CD media is a desirable goal, but proves elusive, particularly for some fastidious cell lines. Although there are ADCF, CD culture media formulations available, many show a decreased performance with the higher degree of chemical definition. One major challenge in this area of media design is the formulation of consistent and robust CD media for those fastidious human cell lines that may be anchorage-dependent and used for vaccine production, such as Vero, MRC-5 and WI-38 human cells. It is anticipated that the systematic approaches that are now being used, particularly with the high-throughput methods, will eventually enable even these cells to feed on a vegetarian, CD diet [1-3].

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