Evaluation Report on Syrian Hamster Embryo Cell Transformation Assay

Norihide Asano[1], Takeki Tsutsui[2], Kohji Yamakage[3], Sachiko Kitamoto[4],
Toshio Kasamatsu[5], Mika Yamamoto[6]

[1] Osaka Shin-Ai College, ex-Nitto Denko Corporation, [2] Nippon Dental University
[3] Hatano Research Institute, Food and Drug Safety Center, [4] Sumitomo Chemical Co., Ltd.
[5] ex-Kao Corporation, [6] Astellas Pharma Inc.

Abstract

Cell transformation assays (CTA) are one method for the *in vitro* assessment of tumor induction potential by measuring adverse effects on cell morphology and phenotypes following exposure to a chemical substance.

JaCVAM Editorial Committee of the SHE Cell Transformation Assay has reported the results of its review of an OECD (Organisation for Economic Co-operation and Development) guidance document released in May 2015,[1)] and other materials related to the usefulness of the Syrian Hamster Embryo Cell Transformation Assay (SHE CTA) as a means of predicting the carcinogenic potential of test chemicals. The SHE CTA is characterized by the use of cells from primary cultures, cells which maintain their basic metabolic capacity, a short culturing period of roughly one week's time, and relatively low test costs, but also the need for a significant level of education and training to enable proper assessment of the transformed cell colonies.

A significant volume of literature related to the SHE CTA and its correlation with carcinogenic potential has been published, and its usefulness has been widely debated. Also, a pre-validation study of this test method was conducted by EURL ECVAM (the European Union Reference Laboratory for Alternatives to Animal Testing). Although only a few chemicals were actually tested, when the study began, there was a type of chemical that was considered a potential non-genotoxic carcinogen. A later reevaluation of the SHE CTA by OECD experts[2)] concluded that no non-genotoxic carcinogens were included. Ultimately, since an official validation with a larger number of test chemicals was never conducted, this test method remains unvalidated.

Despite this, studies performed using both carcinogens and non-carcinogens have yielded results that indicate the SHE CTA demonstrates an accuracy, sensitivity, and specificity as well as rates for both false-negatives and false-positives that are largely concordant with those of animal studies, which leads us to conclude that it provides data at least as useful for predicting carcinogens as that from genotoxicity tests.

That being said, however, it is also true that there are many aspects of the mechanisms involved in cell transformation that have yet to be fully elucidated scientifically, which leads us to conclude that it would not suitable to use the SHE CTA in place of established tests for carcinogenic potential using animals.

Although these problematic aspects of the SHE CTA have yet to be resolved, it remains a useful means of assessing cell transformation, which is an important step in the chemically induced carcinogenic mechanism. And when considered in light of the fact that exposure to carcinogens does increase the number of colonies that exhibit cell transformation, we consider it likely that SHE CTA does predict carcinogens.

In particular, SHE CTA results for chemicals classified as either Group 1 or 2A by the IARC (International Agency for Research on Cancer) correlate well with human carcinogenicity, indicating that SHE CTA could be used in combination with structure-activity relationships to screen suspected car-cinogens, which would contribute significantly to reducing the use of animals. It therefore can be con-sidered an alternative to animal testing in the spirit of the 3Rs. When seen in this light, the SHE CTA has sufficient potential as a means of predicting carcinogenic potential to warrant continued accumula-tion of data.