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The status of human diploid cell strain MRC-5 as an approved substrate for the production of viral vaccines*

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The present communication was written because of the increasing interest of a number of national authorities concerning the status of the human foetal cell strain MRC-5 as a potential substrate for the production of viral vaccines.

These cells have now been officially approved for use in the preparation of viral vaccines; a summary of events leading up to this decision follows.

Detailed information of the origin, propagation, preservation and general characteristics of the cells has been published elsewhere (Minutes of the Sixth Meeting, Cell Culture Committee, 1969; Jacobs, 1970; Jacobs, Jones & Baillie, 1970). A brief summary of the history of the cells is given below.

1. The cells were derived from the lungs of a 14-week-old normal male foetus at our laboratories in 1966.

2. The family history was genetically normal; there was no indication of any congenital abnormalities and no sign of neoplastic disease at abortion. Recent enquiries show that there has been no evidence of congenital abnormality or malignancy in surviving members of the family.

3. A frozen cell stock was prepared from cells which had reached the 7th population doubling. Harvested cells were divided into a number of pools, and 481 ampoules, each containing about 3×10^6 cells, were sealed and stored in liquid nitrogen. Sterility tests were done on cell samples before they were frozen. No antibiotics were added to media used up to this stage or at the time when the cells were harvested and stored.

4. Repeated testing of the cells to establish their characteristics show the following:

(a) the cells attain an average of about 45 population doublings before reaching a stage of senescence;

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(b) they have a stable diploid karyotype and the incidence of chromosomal aberrations conforms to the limits recommended for cells of human origin intended for use in the preparation of viral vaccines for man;
(c) tests for extraneous viruses, mycoplasmas, bacteria and fungi by both *in vivo* and *in vitro* methods and by electron-microscopic studies show no evidence of the presence of these agents;
(d) heterotransplantation studies based on implanting cells into immunesuppressed animals provide no evidence of cells effecting the growth of an invasive nodule;
(e) the cells are susceptible to a wide range of viruses infective for man;
(f) tests for histocompatibility antigens revealed that the antigens HL-A2 and HL-A7 constitute part of the surface antigens of the cell—for comparison, the HL-A2 antigen is also present on the well-characterized WI-38 cell strain but HL-A7 has not been detected on these cells (Minutes of the Seventh Meeting, Cell Culture Committee, 1970).

The Cell Culture Committee of the Permanent Section on Microbiological Standardization of the International Association of Microbiological Societies have considered data on the history and testing of MRC-5 cells. Since this information shows the cells to have fulfilled the minimum requirements for acceptance of a cell strain for use in the production of viral vaccines, and by comparing the data with those concerning the similarly derived WI-38 cell strain already in use for some time as a substrate for producing viral vaccines, the Committee recommended that the MRC-5 strain be considered as a standby to replace the WI-38 strain for vaccine production (Minutes of the Sixth Meeting, Cell Culture Committee, 1970).

In the United Kingdom, the Immunological Products Advisory Committee (IPAC) of the Medical Research Council have noted that the MRC-5 cell strain has been subjected to and satisfies all requirements outlined in the recommended regulations concerning criteria for the acceptability of a serially passaged diploid cell population as a substrate for viral vaccines (Minutes of the Seventh Meeting, Cell Culture Committee, 1970).

Accordingly, the licensing authority of the Department of Health and Social Security have approved the use of MRC-5 cells as a substrate for the production of viral vaccines (IPAC 308).

In practice, MRC-5 cells are being used routinely both for the production of poliomyelitis vaccine (in the United Kingdom) and for pre-production studies in the United Kingdom and other countries in connection with their potential use for preparing other viral vaccines. Their use for the production of interferon is also being investigated.

Addendum. Another cell strain (designated MRC-9) of similar origin has been developed more recently and is now stored at our laboratories. Data on its properties are nearing completion, details of which are intended to be published in the near future.

REFERENCES

Jacobs, J. P., Jones, C. M. & Baillie, J. P. (1970). Characteristics of a human diploid cell designated MRC-5. *Nature* **227**, 168–170.

Jacobs, J. P. (1970). Some comparative characteristics of WI-38 and MRC-5 cells and their suitability for the production of viral vaccines. In *Proceedings Symposium on Human Diploid Cells*, pp. 43–55. Zagreb: Yugoslav Academy of Sciences and Arts.

Minutes of the Sixth Meeting of the Committee on Cell Cultures of the Permanent Section on Microbiological Standardization of the International Association of Microbiological Societies, pp. 4–9. New York, 1969.

Minutes of the Seventh Meeting of the Committee on Cell Cultures of the Permanent Section on Microbiological Standardization of the International Association of Microbiological Societies, pp. 8, 10, 13–15, 54–61. Geneva, 1970.

Minutes of the 46th Meeting Immunological Products Advisory Committee, IPAC/308, pp. 3–4. London, 1973.