

# Development Of Leukimia Vaccines

## Collaboration Between MAKNA and HUKM

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### Introduction:

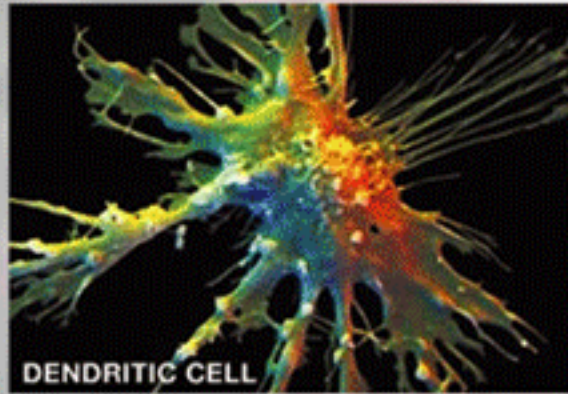
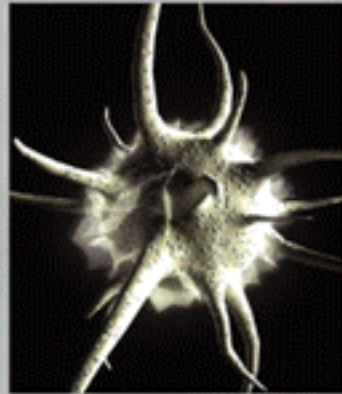
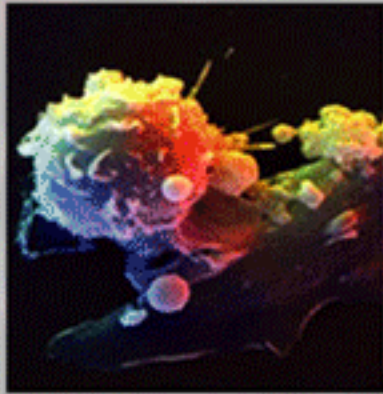
Despite progress in chemotherapy and transplantation, a considerable number of leukemias remains incurable. It is thus necessary to develop alternative strategies, in particular anti-tumor immunotherapy. Increasing the capacity of the immune system to mediate tumor regression has been a major goal in tumor immunology. Progress towards this goal has been recently aided by the identification of immunogenic cancer antigens, and a better understanding of the mechanisms of tumor-specific T-cell immune responses and tumor escape from these responses. Our research proposal is targeted to develop leukemia vaccines that are based on dendritic cells.

### Objectives of The Research:

We propose to generate DC pulsed with tumor cells from peripheral blood or bone marrow of patients with leukemias, and then use these DC for the generation of anti-tumor T cells against the tumor cells. This study will firstly, address the issue of using dendritic cell-based vaccine for immunotherapy of patients with refractory leukemias or relapsed leukemias after stem cell transplant, and secondly identify novel leukemia antigens.

### What Are Dendritic Cells?

- Can be made from monocytes or stem cells.
- If exposed to tumour extract, can capture tumour-specific antigens.
- Had since been shown in animals to cause tumour regression.
- Also inhibit growth of human tumour cell lines.



### Clinical Studies of Anti-Tumor Vaccination With DC:

Since 1999, many of successful use of DC vaccines in B cell Lymphoma, Melanoma, Myeloma, Renal cell Carcinoma, Prostate cancer. Currently, this strategy is actively being pursued in certain centres in Japan, Australia, UK and USA.

### Preclinical Studies of Anti-Tumor Vaccination With DC:

Several studies in mouse tumor models indicate that infusion of DC without loading specific antigens can also decrease growth of tumors to a certain degree.

### Expected Outcomes Of The Study:

1. Dendritic cell based vaccines can be successfully applied to treat selected patients with refractory leukemias and patients who relapse following stem cell transplantation for acute leukemias.
2. Identification of novel leukemic specific antigens which are patentable and of commercial value.

### Justification of the Research:

1. Current treatment of leukemias is still unsatisfactory.
2. Immune tolerance – Tumor immunity is not efficiently induced in tumor-bearing host.
3. Lack of tumor antigen presentation by dendritic cell in vivo is a major problem that can be bypassed by delivery of tumor to autologous dendritic cells ex vivo.
4. Potential commercial value:
  - Development of autologous leukemia DC vaccines for treatment.
  - Identification of novel leukemia antigens which elicit strong cytotoxic T cell responses and these novel antigens are patentable.

### Investigation Setting:

1. Clinical trial of DC vaccine.
  - The clinical trial would be conducted at the Haematology Day Care Center at Hospital UKM. Written consent will be obtained from all patients participating in the trial, regarding the use of leukemic cells to generate DC vaccine from treatment and for identification of leukemia specific antigens.
2. DC vaccine generation and identification of leukemic specific antigens.
  - Preparation of the DC vaccines and also identification of leukemic specific antigens would be carried out in the research laboratories located within the stem cell transplant laboratories, HUKM.

