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COMPARATIVE ASPECTS OF HOST-PARASITE AND HOST-TUMOR RELATIONSHIPS

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FINAL REPORT

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The first session, ^{of the conference} on Interleukin 1, was chaired by Dr. Oppenheim. The discussion dealt initially with the induction of IL-1 by several cell types, and maybe most interesting, induction by injury. Because IL-1 alpha is released more slowly than IL-1 Beta, it was suggested that beta is the intercellular signal and alpha may accelerate subsequent cell mediated reactions. Because IL-1 augments the actions of many cell types in the immune system including antibody production and also the production of other lymphokines, IL-1 has promising therapeutic potential. Dr. Wallach reported that IL-1 prevents bacterial shock by inhibiting the effects of TNF. JES

The second session, Part 1, on Interleukin 2, was chaired by Dr. Smith. There was lively discussion on the interaction of IL-2 with several other lymphokines; IL-1 and IFN alpha being enhancing, and IFN gamma sometimes inhibitory. IL-2 used therapeutically against cancer is probably most effective by increasing the numbers of responding immunocytes. IL-2 has been found to affect only those tumors that cause a local accumulation of immunocytes, among which the T cell is the most likely target.

The second session, Part 2, on Interleukins 4 and 5, was chaired by Dr. Uhr. The most interesting data was the progress in finding inhibitors for IL-4 (to inhibit IgE and allergic reactions) and for IL-5 (to inhibit inflammatory eosinophils). Antibody to IL-5 inhibits eosinophilia in Nippostronsus-infected mice but not high IgE levels. Antibody to IL-4 inhibits IgE production but not eosinophilia.

The third session, Part 1, on Interferon gamma, was chaired by Dr. Nussenzweig. The discussion dealt with distinctions between recombinant human and murine molecules, the mechanism of IFN inactivation, and IFN inhibitors. Inhibitors are eagerly sought, but not yet isolated, with the exception of antibodies produced by Dr. Billiau's group.

The third session, Part 2, on macrophage activating factors, was chaired by Dr. Nancy. The discussion stressed that there are several known macrophage activation factors (IFNg, MCSF, IL-2, IL-4). Which single, or multiple, factor function as activator depends on the nature of the target (nucleated cell or microbe), and on the kind of stimulation the macrophage experiences before exposure to cytokines. Therefore, macrophages have several activation pathways.

The fourth session, on Interleukin 3, was chaired by Dr. Weinstein. It was suggested that the range of activity of IL-3 on hemopoietic cell types was related to its ability to modulate the receptors for various colony stimulating factors. Recombinant IL-3 has also been found to affect B cell differentiation and IgG secretion, comparable to but distinct from IL-6 activity, and likewise at a late stage of B cell activation.

The fifth session, on colony stimulating factors, was chaired by Dr. Stanley. The new information presented was that embryonic myoblasts have CSF-1 receptor m-RNA. This is the only cell outside the trophoblast and macrophage lines described with c-fms. Functional surface expression not yet studied. Mouse fibroblasts may have very small quantities of c-fms. Discussion questioned the latter observation.

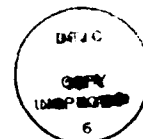
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The sixth session, Part 1, on Interleukin 6, was chaired by Dr. Revel (Dr. Vilcek absent). IL-6 was reported to have a stronger effect on the differentiation and growth inhibition of fresh acute myelogenous leukemia cells, compared to G-CSF and M-CSF. Natural IL-6 had 1/2 the molecular weight of recombinant IL-6, and lower antiviral (IFN-like) activity. IL-6 synergize with IFN gamma and IFN beta for antiviral activity. Murine IL-6, but not human IL-6 has promoted the growth of normal (distinct from transformed) B cells. IL-6 increase antibody production by activated B cells without a shift in antibody isotype composition.

The sixth session, Part 2, on tumor necrosis factor alpha, was chaired by Dr. Wallach. There was extensive and varied discussion, and some of the salient points were:

1. Pretreatment of mice with TNF prevents bacterial shock by inducing anergy to induced TNF.
2. TNF can cure a variety of animal tumors, but has limited effect on mouse mammary tumors.
3. TNF-induced haemorrhagic necrosis is blocked by cobra venom, probably by blocking C5a. Macrophages generate C5a in bacterial infections, which with TNF from macrophages induce neutrophil activation and tissue damage, causing the production of a fibrin barrier against a local infection.

The seventh, and last, session, discussed lymphotoxin and perforin together, and was co-chaired by Drs. Ruddle and Podack. The discussants felt that there is ambiguity about mechanisms of nucleated cell lysis. It was felt that future emphasis should be on the relative importance of perforin and cell mediated lysis compared to other mechanisms.



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