Mechanisms in B-cell Neoplasia. Current Topics in Microbiology and Immunology Vol. 194; Edited by M. Potter and F. Melchers; Springer-Verlag; Berlin, Heidelberg, New York, 1994; xiii + 458 pp. DM 218.00. ISBN 3-540-58447-1

The 12th workshop on 'Mechanisms in B-cell Neoplasia' was held in Bethesda, MD, in June 1994, organised mainly by Dr. Alan Rabson at the National Cancer Institute. A book in the Current Topics in Microbiology and Immunology (CTMI) series (number 194) report from this meeting, edited by Michael Potter and Fritz Melchers.

The main topics covered were multiple myeloma (MM) plasmocytoma, human and mouse B-cell lymphomas, growth regulation (IL-6, c-*myc*, *Bcl*-2, cyclin D1 and ABL) and genomic instability

MM, which is becoming a more common malignant disease, was discussed from many different aspects, including pre-myeloma cells, expressing an Ig idiotype, as initially described by Mellstedt et al (Clin. Exp. Immunol., 17, 371, 1974). These cells were investigated by more sensitive techniques for clonality, including PCR and DNA fingerprinting. These pre-myeloma cells caused a problem in autologous bone-marrow transplantation, due to their ill-defined phenotype marker expression in relation to CD34 expression. An even earlier stage of MM may relate to a condition called Monoclonal Gamopathy of Undetermined Significance (MGUS), ocurring of 3% of the population over 70 years of age. A large percentage of these MGUS patients were reported to develop into MM. Surface Ig on pre-myeloma cells may bind autoantigens and thereby upregulate surface molecules involved in B cell activation and differentiation.

The deregulation of c-*myc* is important in many types of B cell tumors in relation to the cellular control of mitotic cycling and apoptosis. Myc, and myc heterodimers, bind to regulatory motifs in DNA and thus regulate the expression of different genes An increase in c-*myc* also leads to the accumulation of cells in G1/S for further progression to death by apoptosis.

IL-6 was implicated as a growth and maturation factor for plasma cell tumors. IL-6 was found to activate different transduction pathways including immediate JAK-STAT and delayed, *ras*-dependent kinases and CD40-dependent signalling may induce autocrine IL-6 production B cell regulation by IL-6 illustrate the complexity of signalling by cytokines that can modulate transcriptional factors important for terminal differentiation. The importance of IL-6 binding to the IL-6 receptor and signal transducer was approached by isolating a soluble form of the IL-6 receptor (sIL-6R) and anlysing the effect of other growth factors that share the same signal transducer (gp130).

Genomic instability was studied in relation to VDJ rearrangements, and heavy chain isotope switching, and the translocation of other, non-Ig regions, including target genes, such as c-*myc*, *Bcl*-2, *pvt*-1 and others. The PCR technique was used to further characterise chromosomal translocations in relation to the natural history of lymphoma development and the identification of some of these also in non-neoplastic tissues.

Growth regulation by the *Bcl*-2 gene family was discussed. Heterodimerization with Bax was presented as a possible mechanism for *Bcl*-2 to repress cell death. This information needs only to be completed with the latest descriptions of other survival genes, such as *BAG*-1 and *Bad* (Takayama et al., Cell 80:229 and Yang et al., Cell 80.285). *Bcl*-2 overexpression in B-CLL is associated with increased accumulation of B-CLL cells and apoptosis inhibition *Bcl*-2 was proposed to regulate calcium release and to have antioxidant activity to explain its protective potential against different conditions that induce apoptosis

These are just a few of the many reports (54) written by leading workers in the field. The book focuses on important, 'hot' areas in mechanisms in B-cell neoplasia and is a rich source of information both for clinical and basic scientists

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Alzheimer Disease: Therapeutic Strategies; Edited by E. Giacobini and R. Becker; Birkhauser; Boston, 1994; xiv + 509 pp. $ 74.50. ISBN 0-8176-3757-5

Alzheimer's disease (AD) is major cause of dementia, and a major health problem, with suffering both for the affected and their relatives, and enormous costs for the society. The last years have also seen a wealth of studies to characterise the neurochemical pathology of AD. This knowledge forms the platform for therapeutic strategies and attempts to develop new drugs for the disorder. Indeed, *Alzheimer Disease Therapeutic Strategies*, the third publication in a series on Alzheimer therapy, edited by Giacobini and Becker, gives a welcome extensive update on these topics.

The cholinergic hypothesis still has a central role in AD therapeutics, receiving almost half the space in the book. The leading therapeutic approach aiming at increasing cholinergic neurotransmission in AD is by means of cholinesterase inhibitor (ChEI). Indeed, the only registered compound for treatment of the cognitive symptoms in AD is a ChEI, namely tetrahydroaminoacridine, or tacrine. Although 13 chapters go through ChEIs, also other compounds aiming at enhancing the cholinergic system are covered, including several chapters on nicotinic and muscarinic agonists.

However, it is clear that multiple neurotransmitter systems are disturbed in AD One of these is the serotoninergic system, reviewed in the chapter by Gottfries. Patients with AD suffer not only from memory disturbances and other cognitive symptoms, but also from emotional disturbances Treatment with selective serotonin re-uptake inhibitors, such as citalopram, reduce emotional disturbances such as irritability, anxiety, and depression These symptoms may, in the earlier stages of the disorder, often cause more discomfort than the cognitive symptoms.

Other therapeutic approaches in AD includes nootropic, antioxidant and anti-inflammatory agents. In the chapters by McGeer and co-workers and by Webster and Rogers, evidence for an inflammatory component in the pathogenesis is reviewed Interestingly, also a preliminary clinical trial using the non-steroidal anti-inflammatory drug indomethacin, support that anti-inflammatory agents may be beneficial for the treatment of AD.

Several chapters discuss therapeutic strategies aiming at arresting the deposition of amyloid is the brain. The pros and cons concerning the amyloid cascade hypothesis are weighed in the chapter by Hardy and Duff. According to the hypothesis, βA4 protein deposition is the central event in the pathogenesis of AD, which is regarded an amyloid storage disease of the brain Amyloid deposition is regarded to start a cascade of events that finally results in the dementia that brings the patient to the physician. The essential prediction in the amyloid cascade hypothesis is that βA4 protein, or aggregates of βA4 protein, is neurotoxic. This has been both extensively tested (in animal experiments and cell culture systems), and debated (in a whole issue of Neurobiology of Aging) In fact, a book on therapeutic strategies for AD is an excellent forum to discuss the amyloid cascade hypothesis, since the real challenge for the amyloid cascade hypothesis will not come until drugs that (in cell culture or animal models) arrest amyloid deposition can be tested in living patients with AD, to see if they also arrest the progression of the disease.

Nine chapters are devoted to the issue of monitoring the drug by different imaging techniques (e.g. SPECT and PET) and by clinical testing (using different rating scales). However, although evidence are accumulating that what today is called 'Alzheimer's disease' actually is a heterogeneous syndrome, no chapter discuss whether the drug effect may vary between AD patients with different aetiology (e.g. rare genetic forms vs. common sporadic forms) and pathogenesis (e.g. patients with or without risk-factors such as the ApoE4 allele or concomitant vascular diseases). Moreover, it is also logical to assume that the pathogenesis in the rare cases with early-onset sporadic AD (with onset 40–65 years of age) is not identical to that in elderly patients 80–90 years of age (where AD pathology is found in almost all individuals, and 25–40% has dementia). Thus, also the clinical response to different drugs may vary between these patients Consequently, a clinical