



Fig. 1. Inhibition of oncogenes by antineoplastons. Growth factors, such as EGF or PDGF bind to receptors and activates PTK.^[40-42] PTK binds to GRB2 and GNRF.^[43,44] GNRF activates p21 through conversion of GDP (bound to p21) to GTP.^[45] The fusion protein BCR-ABL also has PTK activity.^[46-48] Activation of p21 occurs only after isoprenylation, methylation, and attachment to the membrane, which is blocked by AS5 and AS2-1.^[49-51] p21 localises Raf to the membrane. This activates MAPK, which phosphorylates MAPKs, Erk-1, Myc, and Jun regulating the activity of numerous genes.^[52-54] Abbreviations: see Glossary.

colon, larynx or stomach, and heavy smokers, do not express GSTs encoded by GSTM1 and GSTP1.^[33,71-76] These genes are suppressed by hypermethylation.^[33] A2, A3, A5, AS2-1, and AS5 may play an important part in the prevention and treatment of cancer by decreasing methylation of genes (fig. 2).^[12,26-28,34,37,38,77]

Whatever their detailed mechanism of action, it can be clearly observed that antineoplastons induce abnormal cells to undergo terminal differentiation and die. Dying cells are gradually eliminated and replaced by normal cells, leading to healing of the diseased organ. Once all abnormal cells are elimi-

nated, the disease should be cured. More data on anticancer activity, toxicology, mutagenicity, teratogenicity and pharmacokinetics of antineoplastons are available in the literature.^[4-7,10,14,15,27,28,35,78-119]

2. Treatment with Antineoplastons

2.1 Phase I Studies and Adverse Reactions

Phase I trials with antineoplastons and their active ingredients have been conducted at the National Cancer Institute (NCI), Kurume University School of Medicine in Japan and the Burzynski Research Institute (BRI).^[19,37,38,119-127] In addition,