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Abstract: This is a brief preface and so we have not made a separate abstract section.

Since the sequence of the human genome became available it has been clear that there are four members of the Epidermal Growth Factor receptor family. The HER4 gene is however subject to splicing to produce at least four full length receptor products with varying properties and functions. Defining a limit for the number of ligands is more problematic but there are clearly a minimum of eleven genes. In the case of the Neuregulins 1-4 they are spliced to give a daunting complex array of alternative gene products with unexpected sub-cellular locations and possible functions. Despite this growth in our knowledge in the composition of this highly interactive family it is still not uncommon to see references to "the EGF receptor and its ligands EGF and TGFalpha" in some review articles. This volume goes some way forward in reinforcing the reality that this is a highly complex family of molecules which have critical roles in breast development and in disease. Indeed the work described represents many paradigms which may well apply to less studied receptor tyrosine kinases. The system can be viewed as a computational device existing in cell membranes capable of receiving and integrating a wide array of signals and producing a variety of possible cellular responses. The components of the system, unlike in an electronic computer can vary in expression levels under natural conditions and aberrant over expression or mutational activation can perturb cell behaviour making significant contributions to the carcinogenesis process.

By a deeper understanding of the system we will not only appreciate its role in normal tissue development and function but also its role and relative importance in cancer in general and in individual patients. At present our targeted drugs are only the first generation of possible strategies of intervention and our ability to identify appropriate targets (or combinations of targets), doses, schedules, and indeed patients to treat are rudimentary. It is the belief of those who have worked, sometimes now for their whole careers on this problem, that we can learn much more about the system as a whole so that drug development can be carried out on a more rational and well informed basis.

We thank the Chief Editor David Salomon for selecting us to edit this volume (and for encouragement and occasional arm twisting) but we thank most of all the authors of these articles for obeying our outrageously short deadlines and delivering such erudite and readable reviews. There may be much more to be done but there are clearly scientists old and new to the field who can do the job.

WJG/FJ