Partial Amino Acid Sequences of \(\kappa\)-Chains of Rat Immunoglobulins: Genetic and Evolutionary Implications

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Partial amino acid sequences have been determined for several \(\kappa\)-type light chains prepared from sera or urine of inbred LOU/C\(\bar{W}\)sl rats bearing plasma cell tumors. Comparison of these sequences with those of human, rabbit, and mouse \(\kappa\)-chains available in the literature indicates that the constant region of rat \(\kappa\)-chains shows more amino acid sequence homology to that of the mouse \(\kappa\)-chain than to human and rabbit \(\kappa\)-chains, a result expected from the phylogenetic relationship of the species compared. Examination of the N-terminal amino acid sequences indicated that the variable regions of rat \(\kappa\)-chains can also be classified into subgroups according to degree of sequence homology in a manner similar to that done for \(\kappa\)-chains of other species (e.g., human, rabbit, and mouse). However, the prototype amino acid sequences of \(\kappa\)-chain variable region subgroups of the rat were not homologous to those of other species including the closely related mouse. The implications of this observation with respect to the genetics and evolution of immunoglobulins are discussed.

KEY WORDS: immunoglobulins; amino acid sequence; genetics and evolution.

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INTRODUCTION

Immunoglobulins (Ig) are highly heterogeneous. Each Ig molecule has one or more four-chain basic units which consist of two identical light (L) and two identical heavy (H) polypeptide chains (Gally and Edelman, 1972; Porter, 1973). The Ig polypeptide chains are folded into repeating homology units designated as domains (Poljak et al., 1974; Putnam, 1974). Each domain is approximately 110 amino acids in length and has an intrachain disulfide bond connecting two cysteine residues which are approximately 60 amino acid residues apart. It has generally been accepted that all existing Ig genes have evolved by repeated gene duplication and fusion from a common ancestral gene coding for a polypeptide chain which is equivalent to a domain (Hill et al., 1966; Singer and Doolittle, 1966; Smith et al., 1971). Amino acid sequence studies of monoclonal Igs indicated that two genes are involved in the synthesis of each Ig polypeptide chain, one gene coding for the constant (C) region and another coding for the variable (V) region of each chain (Dreyer and Bennett, 1965; Wang et al., 1970). Serological, biochemical, and pedigree studies showed that multiple genes control the production of both the C and the V regions of both the L and H chains. However, the "number" of V-region genes is still a controversial issue (Fudenberg et al., 1972; Gally, 1973; Hood, 1973).

Three major hypotheses have been proposed attempting to explain the genetic control of antibody variability. These are the somatic mutation (Lederberg, 1959; Brenner and Milstein, 1966; Jerne, 1971; Franek and Novotny, 1972; Capra et al., 1973), the somatic recombination (Edelman and Gally, 1967; Smithies, 1967), and the germ-line (Dreyer and Bennett, 1965; Hood and Talmage, 1970) hypotheses. Both somatic hypotheses propose that each V-region subgroup is coded for by a single gene (or a small number of genes) and that antibody variability is generated by mutation or recombination in somatic cells. In contrast, the germ-line hypothesis proposes that the V-regions of each antibody are coded for by a specific pair of $V_H$ and $V_L$ genes, and that each individual has 1000 or more V-region genes in the genome.

Previously, most of the structural studies on Igs were done on monotypic proteins derived from plasma cell tumors in man and mouse (Potter, 1967). Similar studies in other species were hampered by the fact that homogeneous Igs were generally unavailable except in the rabbit. In this species, a great deal of effort has been made by many investigators for the preparation of homogeneous antibodies.

Bazin et al. (1972, 1973) discovered that plasma cell tumors are transplantable in rats. The availability of monotypic Igs in rats offered a good opportunity to study the evolution of Ig polypeptide chains. The present report compares amino acid sequences of rat $\kappa$-chains with those of a closely