Evolution of the Glycophorin Gene Family in the Hominoid Primates

Ann Rearden,1,2 Huan Phan,1 Shinichi Kudo,3 and Minoru Fukuda3

Received 30 Oct. 1989—Final 2 Feb. 1990

Analysis of nucleotide sequences of the human glycophorin A (GPA) and glycophorin B (GPB) genes has indicated that the GPA gene most closely resembles the ancestral gene, whereas the GPB gene likely arose from the GPA gene by homologous recombination. To study the evolution of the glycophorin gene family in the hominoid primates, restricted DNA on Southern blots from man, pygmy chimpanzee, common chimpanzee, gorilla, orangutan, and gibbon was probed with cDNA fragments encoding the human GPA and GPB coding and 3'-untranslated regions. This showed the presence in all of the hominoid primates of at least one GPA-like gene. In addition, at least one GPB-like gene was detected in man, both chimpanzee species, and gorilla, strongly suggesting that the event that produced the GPB gene occurred in the common ancestor of man–chimpanzee–gorilla. An unexpected finding in this study was the conservation of EcoRI restriction sites relative to those of the other four enzymes used; the significance of this observation is unclear, but raises the question of nonrandomness of EcoRI restriction sites in noncoding regions. Further analysis of the evolution of this multigene family, including nucleotide sequence analysis, will be useful in clarification of the evolutionary relationships of the hominoid primates, in correlation with the structure and function of the glycophorin molecules, and in assessment of the role of evolution in the autogenicity of glycophorin determinants.

This work was supported in part by National Institutes of Health Grants AM33463 and CA33000.

1 Department of Pathology, M-012, University of California San Diego, La Jolla, California 92093.
2 To whom correspondence should be addressed.
3 La Jolla Cancer Research Foundation, Cancer Research Center, La Jolla, California 92037.
INTRODUCTION

In man, the principal sialoglycoproteins of the red cell membrane are glycophorin A (GPA) and glycophorin B (GPB). Variability in antigen content of the glycophorin molecules in the hominoid primates has been shown with a panel of 10 monoclonal antibodies to human glycophorin determinants (Rearden, 1986); common and pygmy chimpanzee red cells were agglutinated by 8 antibodies, gorilla by 6, orangutan by 5, and gibbon by 2. This observation suggested that glycophorins might be a useful model to study evolutionary differences among the hominoid primates.

Analysis of the structure of the human GPA and GPB genes has shown that the genes are homologous from the 5' flanking region to 1.0-kb downstream from the exon encoding the transmembrane region (Kudo and Fukuda, 1989). Analysis of direct repeats flanking the Alu sequences at the transition sites suggests that GPA most closely resembles the ancestral gene, whereas GPB arose by homologous recombination at the Alu repeats during or after gene duplication, and acquired 3'-end sequences from an unrelated gene.

To define further the evolution of the glycophorin gene family, restricted DNA from the hominoid primates on Southern blots was probed with DNA fragments encoding the human GPA and GPB coding regions and their respective 3'-untranslated regions.

MATERIALS AND METHODS

Human and Primate Bloods. Peripheral bloods (17–34 ml) from three pygmy chimpanzees (Pan paniscus), four common chimpanzees (Pan troglodytes), seven gorillas (Gorilla gorilla), five orangutans (Pongo pygmaeus), and five gibbons (Hylobates lar) were obtained from the Yerkes Regional Primate Research Center, Emory University, Atlanta, Georgia, through the courtesy of Dr. Harold McClure. Blood (20–30 ml) from an additional nine common chimpanzees (Pan troglodytes) was obtained from the Laboratory for Experimental Medicine and Surgery in Primates of the New York Medical Center, through the courtesy of Dr. Wladyslaw W. Socha. Bloods were collected in acid–citrate–dextrose, shipped overnight, and used the following day. Primate bloods were obtained with the approval of the University of California San Diego Animal Subjects Committee. Human peripheral blood was obtained under conditions approved by the University of California San Diego Human Subjects Committee.

Preparation of DNA. Whole-blood samples were centrifuged at 1000g for 10 min. The "buffy coat" layer of white cells (slightly contaminated with