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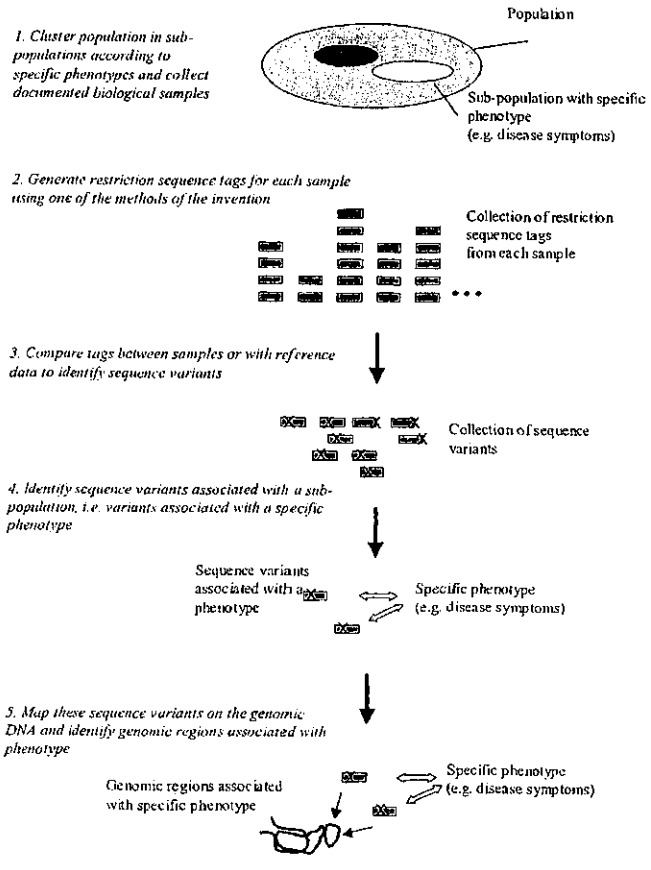
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(54) Title: METHODS FOR DETECTING GENOME-WIDE SEQUENCE VARIATIONS ASSOCIATED WITH A PHENOTYPE



(57) Abstract: The invention provides methods for determining genome-wide sequence variations associated with phenotype of a species in a hypothesis-free manner. In the methods of the invention, a set of restriction fragments for each of a sub-population of individuals having the phenotype are generated by digesting nucleic acids from the individual using one or more different restriction enzymes. A set of restriction sequence tags for the individual is then determined from the set of restriction fragments. The restriction sequence tags for the sub-population of organisms are compared and grouped into one or more groups, each of which comprising restriction sequence tags that comprise homologous sequences. The obtained one or more groups of restriction sequence tags identify the sequence variations associated with the phenotype. The methods of the invention can be used for, *e.g.*. analysis of large numbers of sequence variants in many patient samples to identify subtle genetic risk factors.

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