UNRAVELING THE TERMINAL STEPS IN RUBBER BIOSYNTHESIS: CURRENT PERSPECTIVES ON THE ROLE OF *CIS*-PRENYLTRANSFERASE AND *HEVEA* RUBBER TRANSFERASE 1 - REF BRIDGING PROTEIN

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Natural rubber, predominantly synthesized by *Hevea brasiliensis*, is a vital biopolymer with unique physicochemical properties essential to numerous industries. Despite its economic importance, the enzymatic mechanism, underlying its biosynthesis is not yet fully elucidated. While the upstream steps leading to isoprene monomer production mediated predominantly *via* the mevalonate (MVA) pathway are relatively well understood, the downstream polymerization processes responsible for assembling these monomers into high molecular weight polyisoprene with the characteristic chain length of natural rubber remain poorly characterized. Available information suggests that *cis*-prenyltransferases (CPTs) and other proteins like Rubber Elongation Factor (REF) and SRPP (Small Rubber Particle Protein) which, together with the HRT1-REF bridging protein (HRBP), form a functional rubber transferase complex on the surface of rubber particles which facilitates the chain elongation. While CPT is known to interact with REF and SRPP, HRBP is thought to stabilize the above complex on the surface of rubber particles facilitating the polymerization of isopentenyl pyrophosphate (IPP) into high molecular weight polyisoprenes. Current research has identified and cloned several isoforms of CPT and HRBP and their expression profiles suggest tissue-specific and developmentally regulated roles in latex-producing cells. Additionally, functional studies including heterologous expression in yeast and other model systems have demonstrated the catalytic potential of these enzymes. However, the exact molecular mechanisms and the specific role of different variants of these enzymes and their inter-regulatory mechanism leading to IPP chain initiation, elongation and termination still remains unresolved. This review discusses the various studies on CPT and HRBP, the two critical genes in the above process and prospective approaches including structural biology, *in vitro* reconstitution and synthetic biology that may bridge the current knowledge gaps and enable the engineering of rubber biosynthesis mechanism for crop improvement in *Hevea* as well as in the evolvement of *in vitro* biological systems for rubber synthesis.

Keywords: *Cis*-prenyltransferase, *Hevea* rubber transferase 1 (HRT1)-REF bridging protein, Rubber biosynthesis, Rubber particle

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