Tuberous Sclerosis Complex

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KEYWORDS

- Neurocutaneous • Neurogenetic • Tuberous sclerosis complex
- Subependymal giant cell astrocytoma • Epilepsy • Autism
- Mechanistic target of rapamycin (mTOR) • Rapamycin

KEY POINTS

- Hypopigmented macules in the skin coupled with either epilepsy or autism are important diagnostic findings.
- Prenatal identification of a cardiac rhabdomyoma is a common early presenting manifestation.
- Hyperactivity of the mechanistic target of rapamycin complex 1 (mTORC1) constitutes the molecular basis of tuberous sclerosis complex (TSC).
- Symptomatic treatments as well as molecular-targeted therapy with current mTORC1 inhibitors are treatment options.
- The mTORC1 inhibitor, everolimus, is approved by the US Food and Drug Administration for the treatment of renal angiomyolipomas that do not require immediate surgery in adults with TSC and subependymal giant cell astrocytomas that cannot be surgically resected in adults or children with TSC.

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INTRODUCTION

Tuberous sclerosis complex (TSC) is an autosomal-dominant, neurocutaneous, multisystem disorder characterized by cellular hyperplasia and tissue dysplasia.[1,2] The disease has 2 known genetic loci: *TSC1*, found on chromosome 9q34; and *TSC2*, found on chromosome 16p13.[2–4] Clinical phenotypes resulting from mutations in either of these genes are variable.[5–9]

EPIDEMIOLOGY

TSC can be identified in all ethnic groups and is equally identified in both sexes. Population studies have estimated a prevalence of 1 in 6000 to 9000 people. Although TSC is an autosomal-dominant inherited disorder, up to 65% to 75% of people affected with TSC have had spontaneous mutations. An estimated 40,000 Americans and at least 2 million people worldwide are affected with TSC.[2]

CAUSE

TSC can be caused by mutations in 2 different genes: the *TSC1* gene, found on chromosome 9q34; and the *TSC2* gene, found on 16p13.[2–4] The *TSC2* gene accounts for as many as 90% of the clinical cases; however, mutations in both TSC1 and TSC2 may produce the same phenotype, varying from individual to individual.[5–7] This genetic heterogeneity is made more complex by variable clinical expression even with the same genetic mutation within a given family (**Figs. 1–12**).[7]

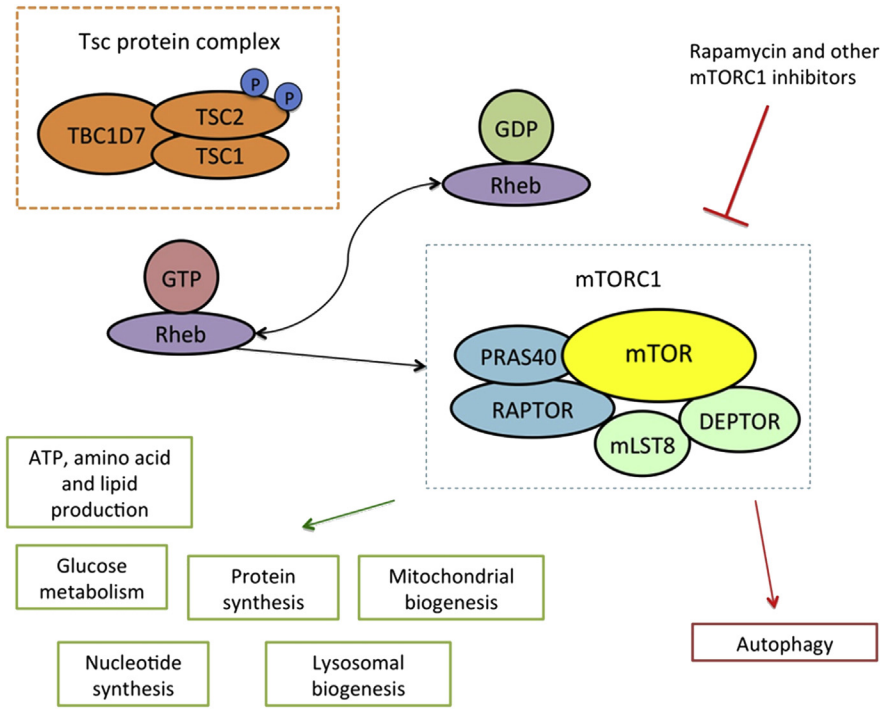

Fig. 1. TSC protein complex and mTOR signaling.