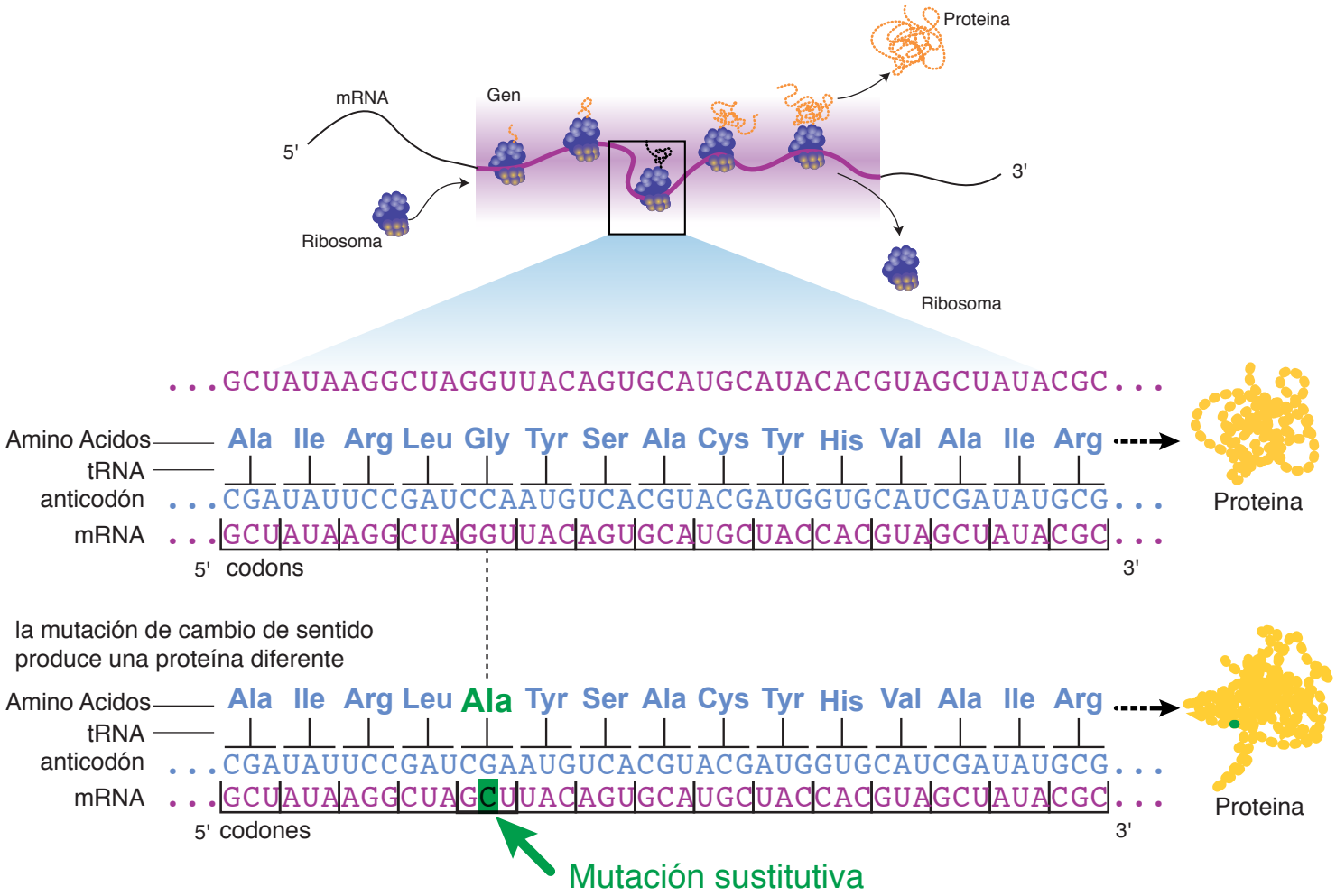Mutación sustitutiva