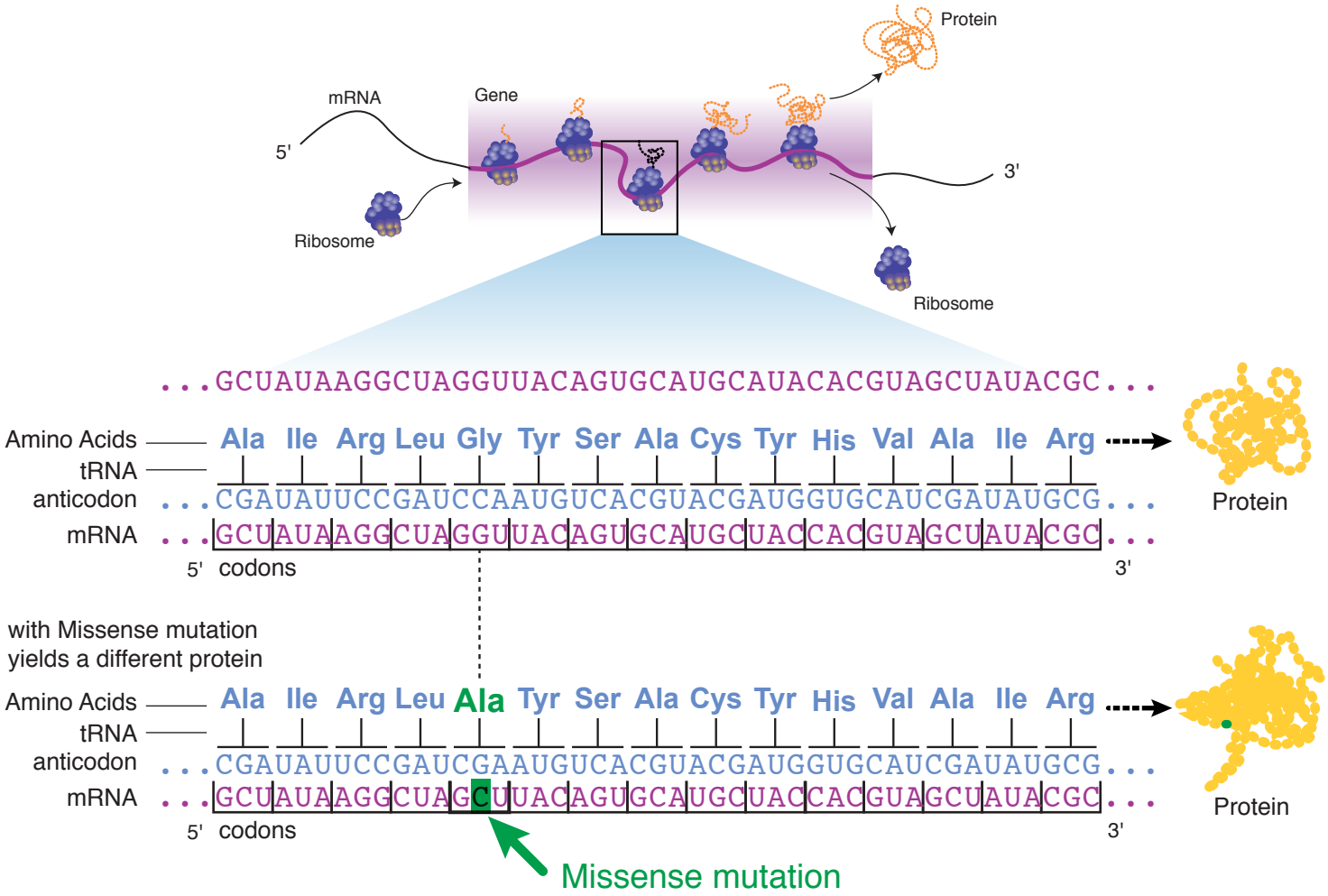Missense mutation