

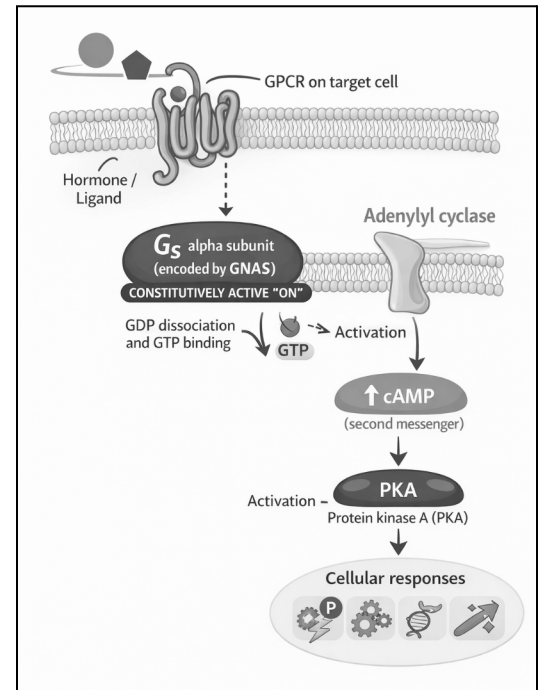
## BC368 - Biochemistry of the Cell II Case Study #3

### Background:

A 22 month old girl is referred to your hospital with complaints of **early breast development** and **recurrent vaginal bleeding** over the past several months. The family also reports that the patient has **poor sleep**, **excessive sweating**, and episodes where she appears to have a **racing heart**. The presence of peripheral precocious puberty and hyperthyroid symptoms leads to a suspicion of **McCune-Albright syndrome (MAS)**.

### Biochemistry:

In MAS, the defect is the mutation in the GNAS gene. This gene encodes the Gs alpha subunit ( $G_{\alpha_s}$ ), a key component in the G-coupled receptor signaling pathway. The mutation inhibits GTPase activity which forces  $G_{\alpha_s}$  to remain **constitutively active**. This causes a flood in cAMP, leading to the constitutive activation of Protein Kinase A (PKA). PKA then phosphorylates various target proteins leading to a constant cellular response even in the absence of an external hormonal signal.



### Lab Results:

Before treatment, labs were ordered to confirm if MAS is the true culprit of the symptoms as shown below:

Test	Patient value	Flag	Role
<b>Precocious Puberty Indicators</b>			
LH	< 0.1 IU/L	SUPPRESSED	Pituitary driver signals to the ovary to stimulate E2
FSH	< 0.1 IU/L	SUPPRESSED	
Estradiol (E2)	2690 pmol/L	HIGH	Causes breast development/bleeding
<b>Hyperthyroidism Indicators</b>			
TSH	< 0.01 mIU/L	SUPPRESSED	Pituitary driver signal to the thyroid to stimulate Free T4
Free T4	25.5 pmol/L	HIGH	Excess causes hyperthyroidism

**Question 1.** *Based on the description of McCune-Albright syndrome along with the lab results, do you think the initial diagnosis was correct? Why?*

**Treatment:**

In endocrine disorders, there are a multitude of levels of a signaling pathway that could be targeted: blocking the receptor, interrupting intracellular signaling, or reducing the final hormone produced by the target gland. You decide to treat the patient by prescribing Letrozole and Carbimazole to address the issues of precocious puberty and hyperthyroidism respectively.

**Question 2.** *What mechanism should the given drugs target for it to be effective? Explain why your chosen method beats the alternatives.*

In another similar case, a doctor believes that targeting cAMP by using the *hypothetical* drug cAMP killer (CK) would be an effective way of treatment by regulating the downstream effects. Within the first 2 weeks, conditions drastically improve, however around 6-8 weeks the symptoms return to baseline despite continued use of CK.

**Question 3.** *What adaptation is occurring in the body that is making the effectiveness of CK worsen as it is used. Hint: think back to yesterday' class, specifically in relation to the opioid example.*

**Key Words:**

GNAS gene, “GTP switch”, cAMP, AC, Constitutive Activation

**Sources**

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2. Millard, Julie. “Transport Across Membranes: Part I and Biosignaling II.” PowerPoint slides. Powerpoint slides. Accessed February 19, 2026.  
<https://web.colby.edu/bc368/course-materials/>.