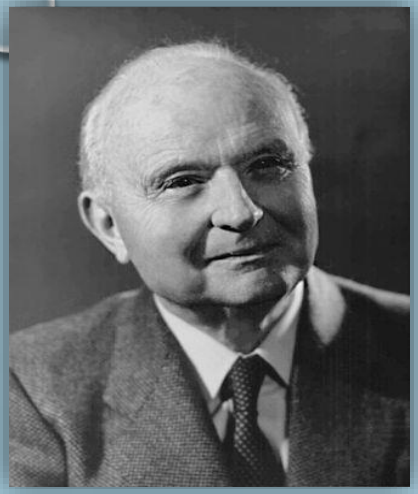
Biochemical of hormones

Ferdowsi University of Mashhad

Reihaneh Feizolah

History

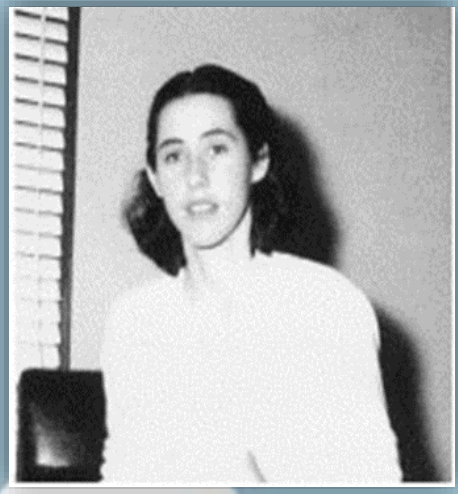


Vittorio Erspamer
1935

- **Enteramine**

Maurice M. Rapport, Arda Green, Irvine Page
1948

- **Serotonin**



Betty Twarog, Page
1952

- **CNS**

- en.wikipedia

Function

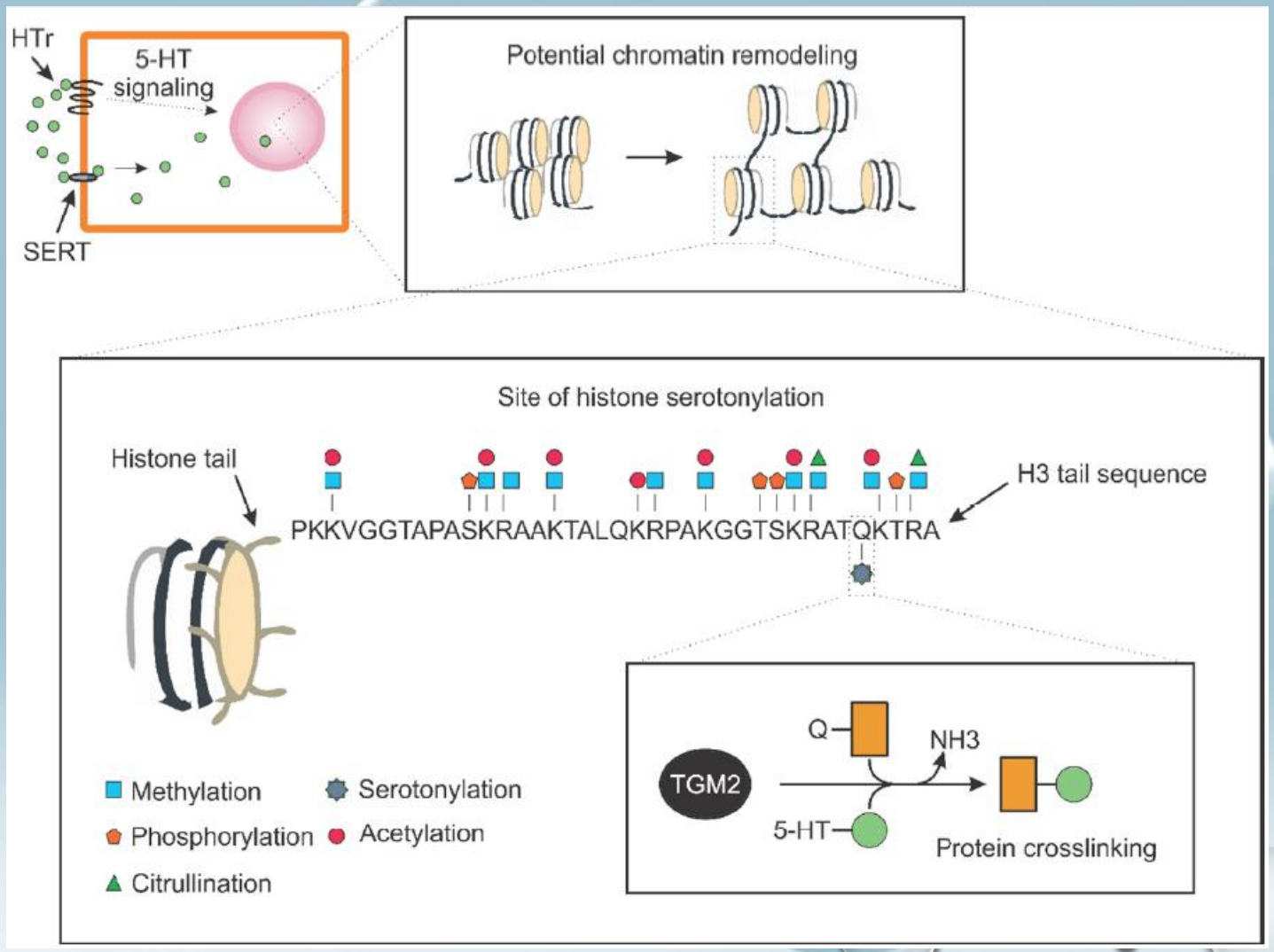
- ✓ Mood ,feeling ,happiness
- ✓ Sleep-wake cycle
- ✓ Appetite
- ✓ Cardiovascular function
- ✓ Sexual behaviors
- ✓ Modulates motility and digestive functions in GI
- ✓ Platelet serotonin promotes aggregation and clotting
- ✓ Secretagogue
- ✓ Serotonylation and exerts epigenetic effects
- ✓ Covalent linkage of serotonin molecules to small GTP-binding proteins(Rho,Rab)

TEM 1516 No. of Pages 15
ARTICLE IN PRESS
Trends in Endocrinology & Metabolism
CellPress REVIEWS

Review

The Dual Role of Serotonin in Colorectal Cancer

Vinicius Kannen,[1,2,*] Michael Bader,[3,4,5] Juliana Y. Sakita,[2] Sergio A. Uyemura,[6] and Jeremy A. Squire[2,7]



Location of Synthesis and Secretion

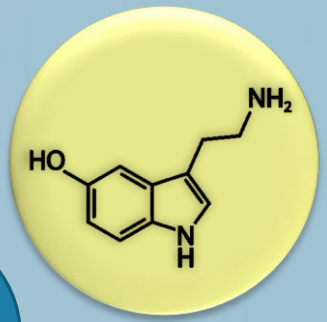
- Gastrointestinal tract, enterochromaffin cells >80%
- CNS contains less than 2%

  serotonergic neurons are clustered in the midline raphe nuclei of the brainstem

- Peripheral serotonin is located in platelets, mast cells

Structure and Metabolism

- Serotonin or 5-hydroxytryptamine (5-HT) is a monoamine neurotransmitter
- Synthesized from the L-tryptophan (from the diet)
- Rate-limiting step: tryptophan hydroxylase (2 isoforms)



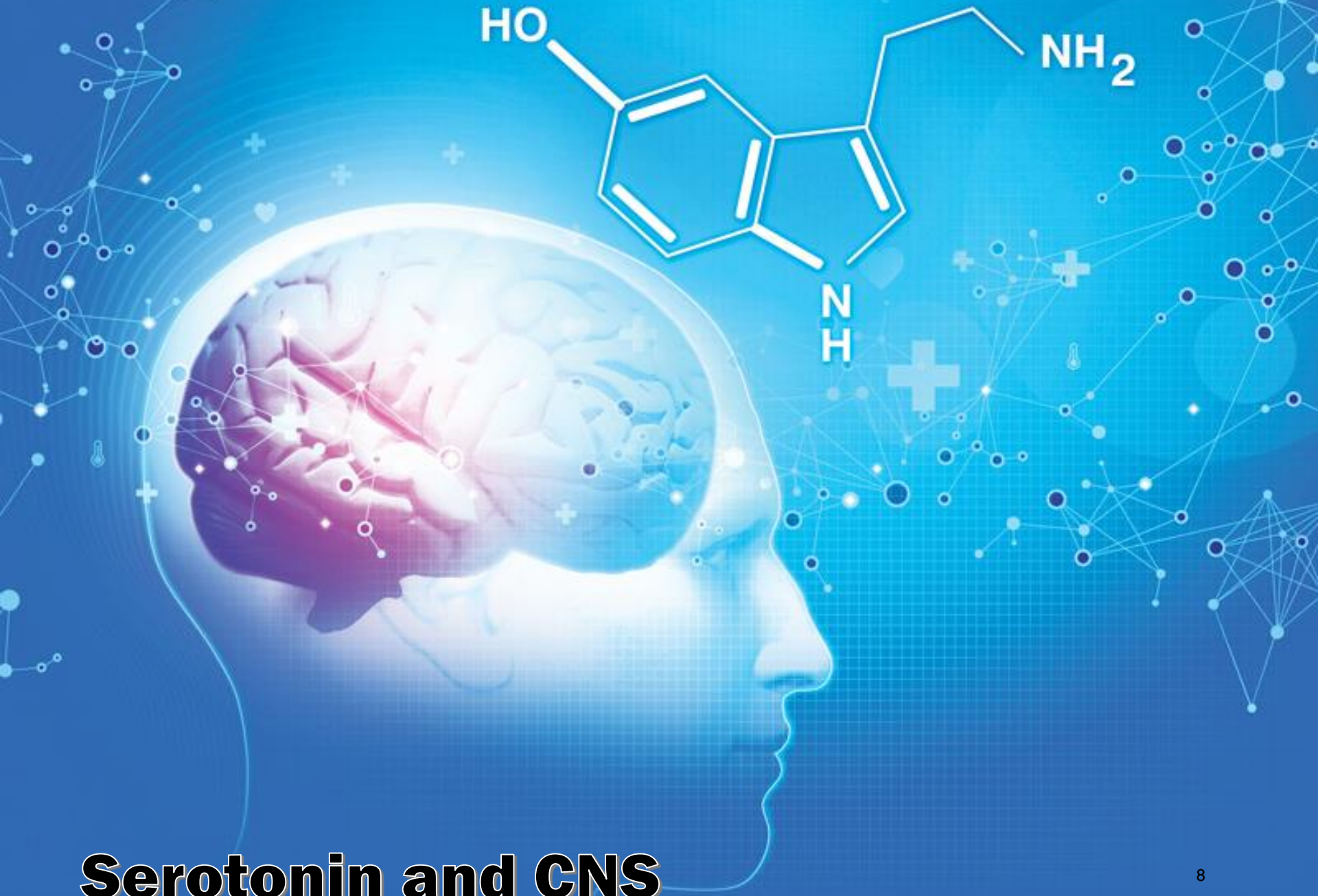
L-tryptophan

↓ Tryptophan hydroxylase

L-5-Hydroxytryptophan

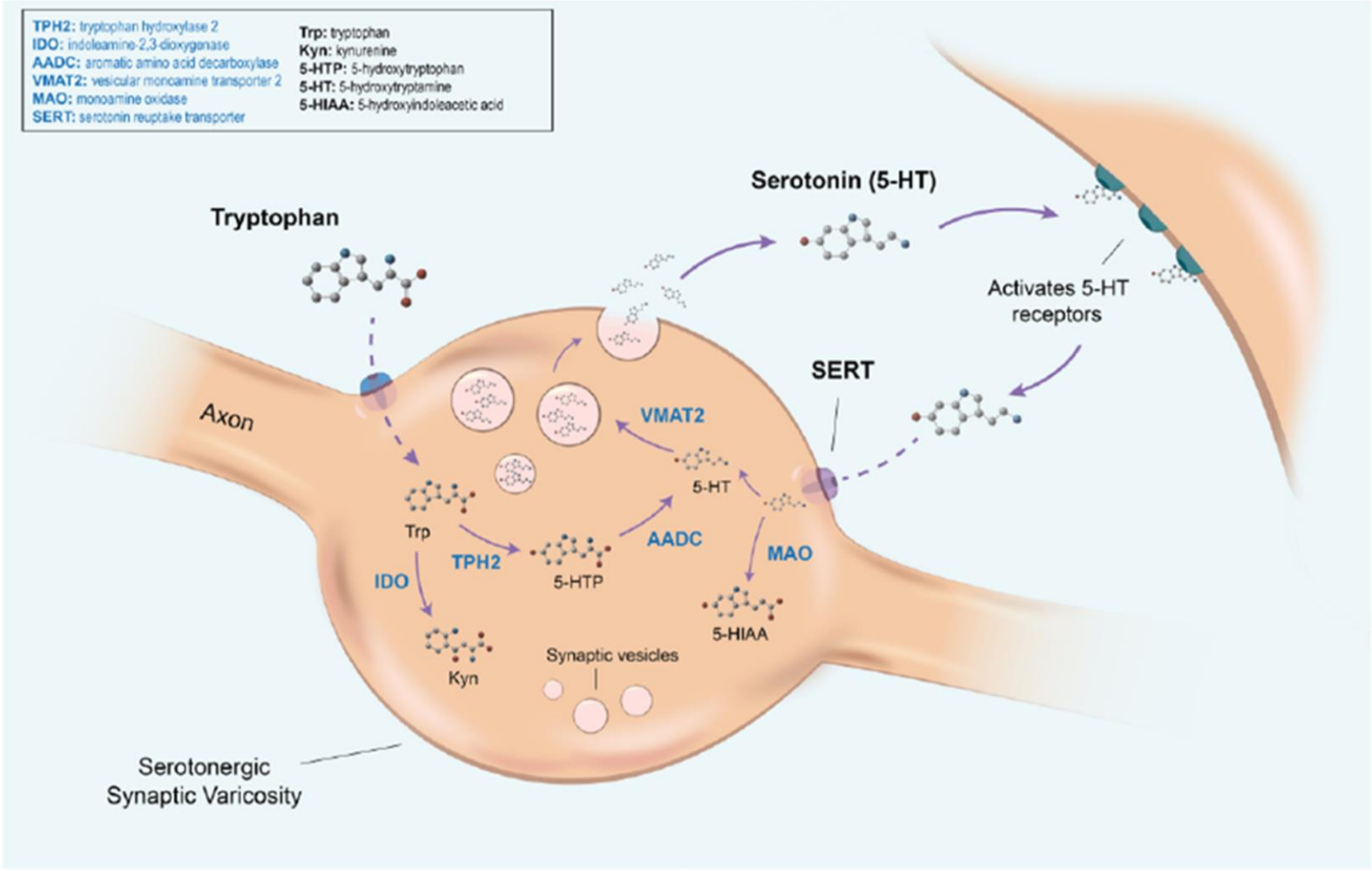
↓ Aromatic L-amino acid decarboxylase

5-Hydroxytryptamine (Serotonin, 5-HT)

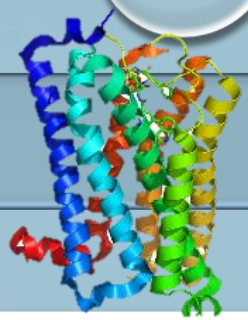


Serotonin and CNS

Metabolism of serotonin in serotonergic neurons



Serotonin Receptors



Serotonin Receptors	Subtypes	Major Signaling pathways	Potential	Major distributions and functions of the Serotonin Receptors
5-HT_1	5-HT_{1A}, 5-HT_{1B}, 5-HT_{1D}, 5-ht_{1E}, 5-ht_{1F}	cAMP↓	inhibitory	Blood vessels, CNS
5-HT_2	5-HT_{2A}, 5-HT_{2B}, 5-HT_{2C}	IP_3↑	Excitatory	Blood vessels, CNS, PNS, Gastrointestinal tract, Platelets, smooth muscle
5-HT_3	5-HT_{3A}, 5-HT_{3B}	Ion Channel	Excitatory	Gastrointestinal tract, CNS (area postrema related to vomiting), PNS
5-HT_4		cAMP↑	Excitatory	Gastrointestinal tract,CNS, PNS
5-HT_5	5-HT_{5A}, 5-HT_{5B}	cAMP?	Inhibitory	CNS
5-HT_6		cAMP↑	Excitatory	CNS (mainly throughout limbic system)
5-HT_7		cAMP↑	Excitatory	CNS (mainly throughout limbic system), blood vessels, gastrointestinal tract

5-HT 2C: many CNS regions; anxiogenic and anorectic effects; regulates neuronal network excitability

Pharmacological compound and Antidepressant Medications

TABLE 3-3 Some Pharmacological Compounds That Alter Indolamine Activity

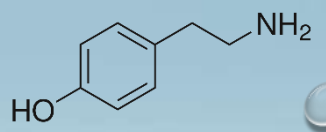
Compound	Action
Fenfluramine	Blocks reuptake of serotonin by presynaptic neurons
Fluoxetine	Selective serotonin reuptake inhibitor (SSRI)
Harmaline	Inhibitor of monoamine oxidase (MAO), an important enzyme for degradation of indoleamines
Lysergic acid diethylamide	Antagonist of serotonin at receptor sites
Methysergide	Antagonist of serotonin at receptor sites

- ✓ Selective Serotonin Reuptake Inhibitor (SSRIs)
- ✓ MAO inhibitor

- ✓ Fluoxetine (Sarafem, Prozac)
- ✓ Sertraline (Zoloft)

- ✓ All SSRIs may cause insomnia, agitation, sedation, GI distress and sexual dysfunction

- ✓ Tyramine



- ✓ Methamphetamine

Huang *et al. EJNMMI Research* (2019) 9:92
https://doi.org/10.1186/s13550-019-0557-y

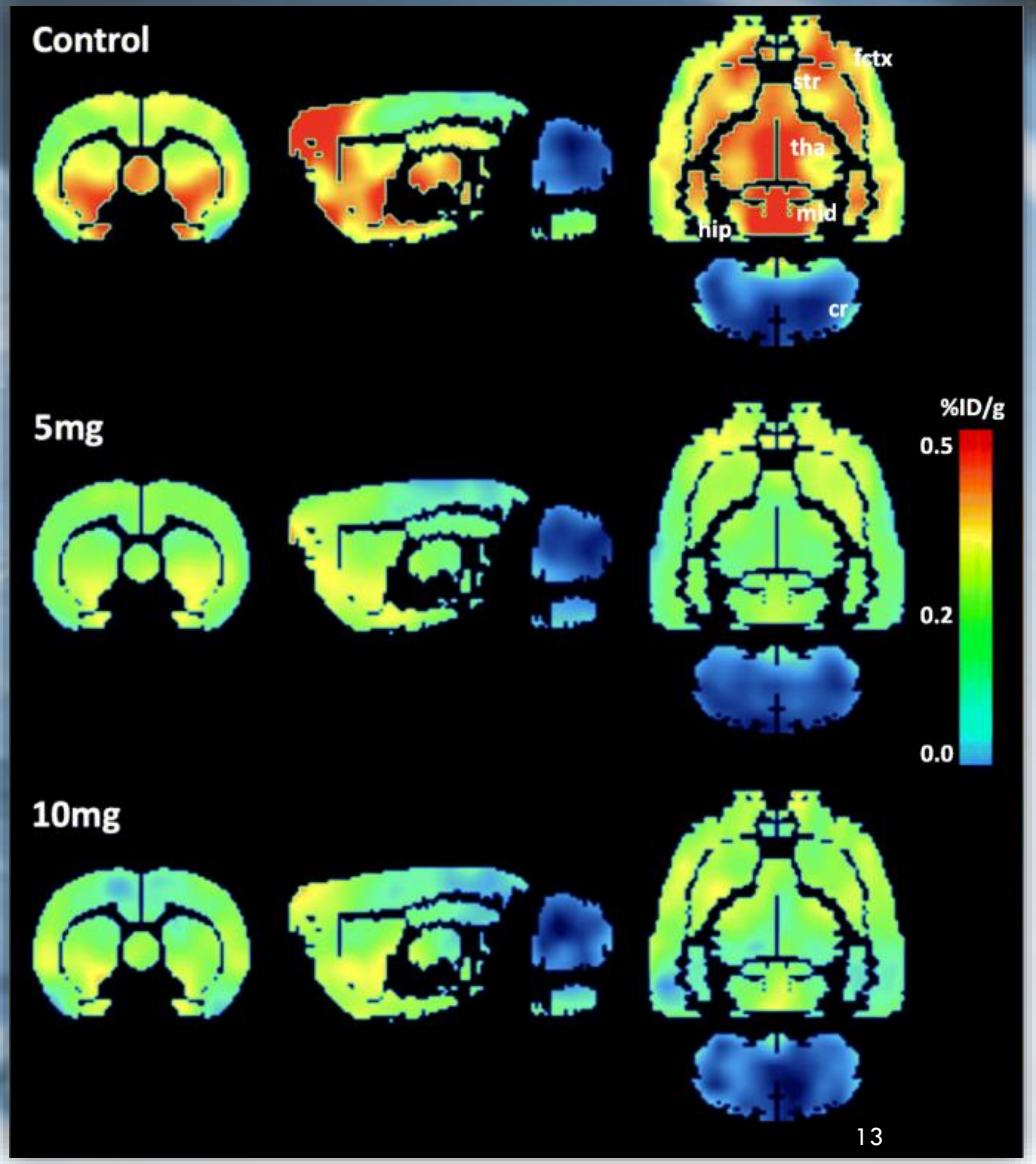
EJNMMI Research

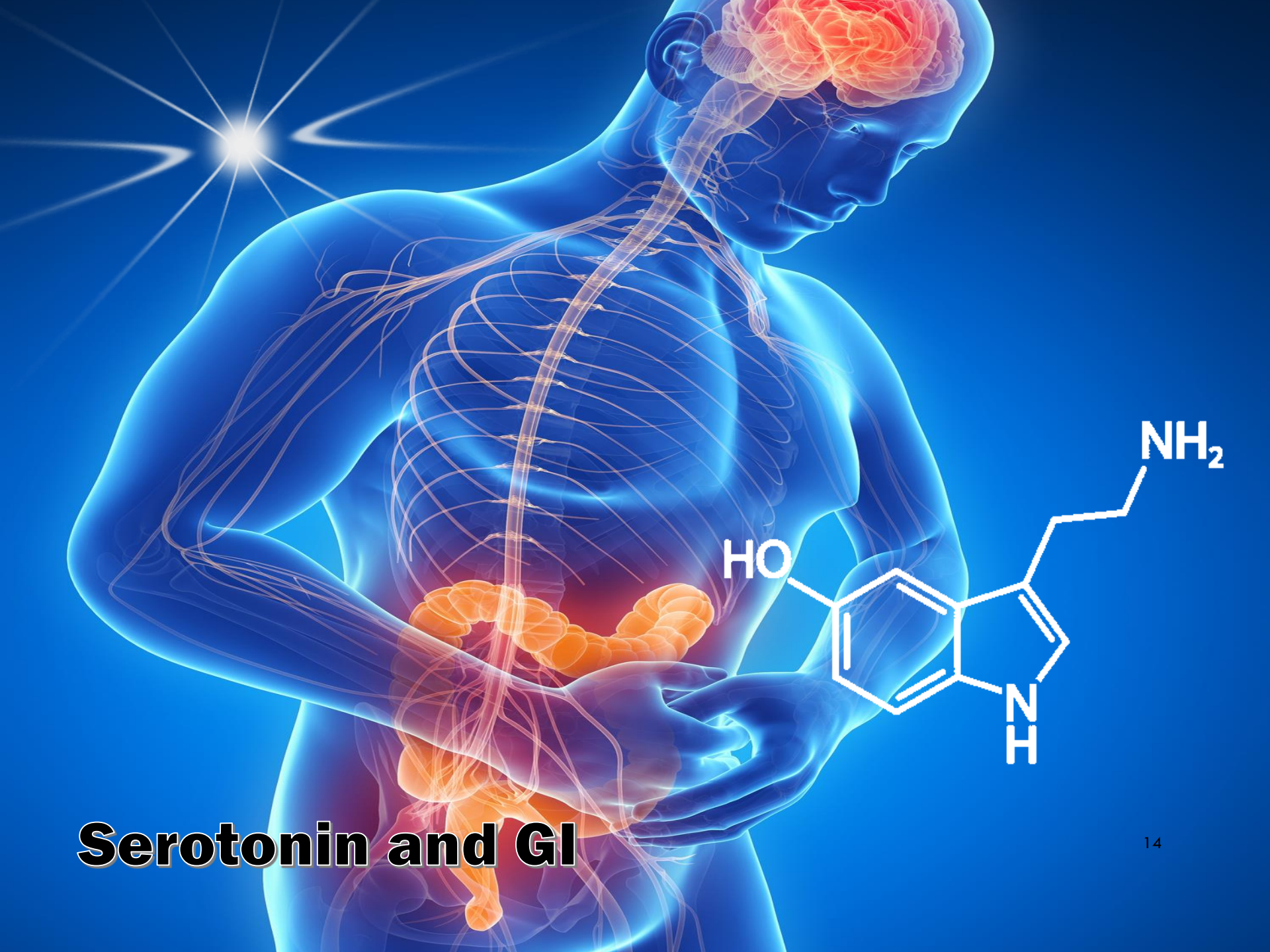
ORIGINAL RESEARCH Open Access

In vivo long-lasting alterations of central serotonin transporter activity and associated dopamine synthesis after acute repeated administration of methamphetamine

Wen-Sheng Huang[1,4], Guann-Juh Chen[2,3], Tung-Han Tsai[2], Chen-Yi Cheng[4], Chyng-Yann Shiue[5], Kuo-Hsing Ma[6*] and Skye Hsin-Hsien Yeh[7*]

- SERT availability/activity using 4-[18F]-ADAM/ Micro-PET imaging
- At 30 days post-administration
- dose/tissue gram (%ID/g)
- Reduced in midbrain, hypothalamus, thalamus, striatum, hippocampus, and frontal cortex.





Serotonin and GI

Autonomic Neuroscience: Basic and Clinical 153 (2010) 47–57

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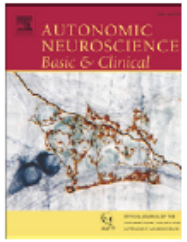

Serotonin release and uptake in the gastrointestinal tract

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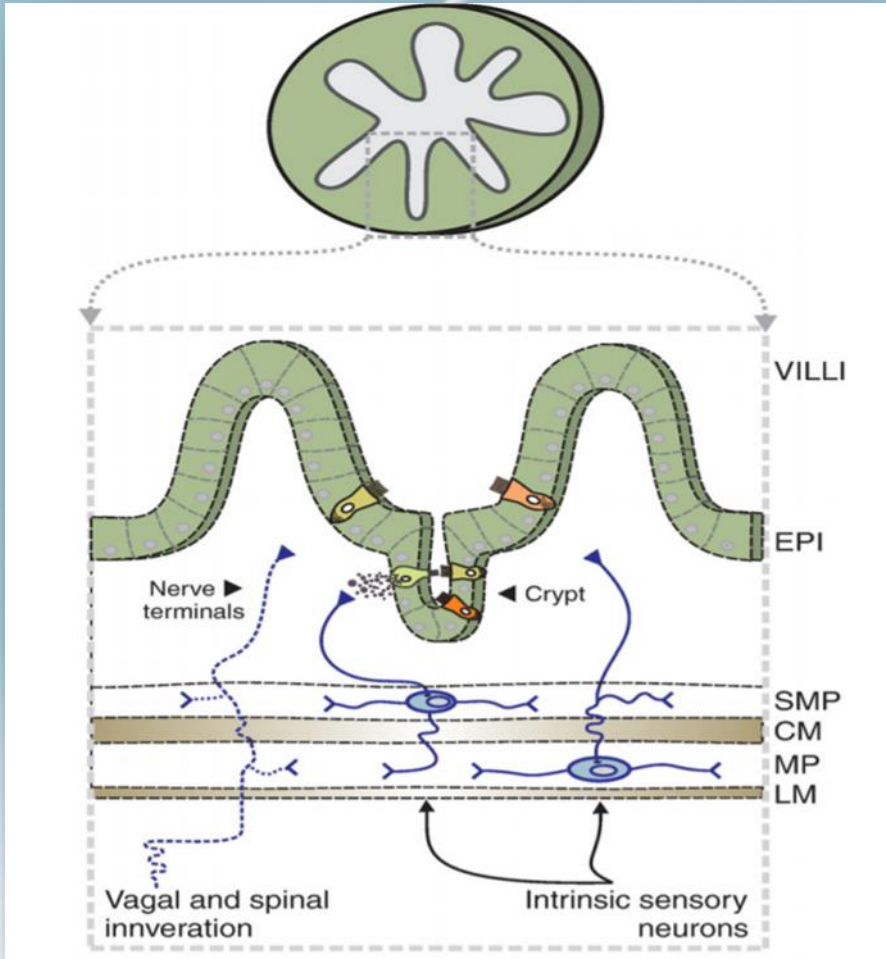
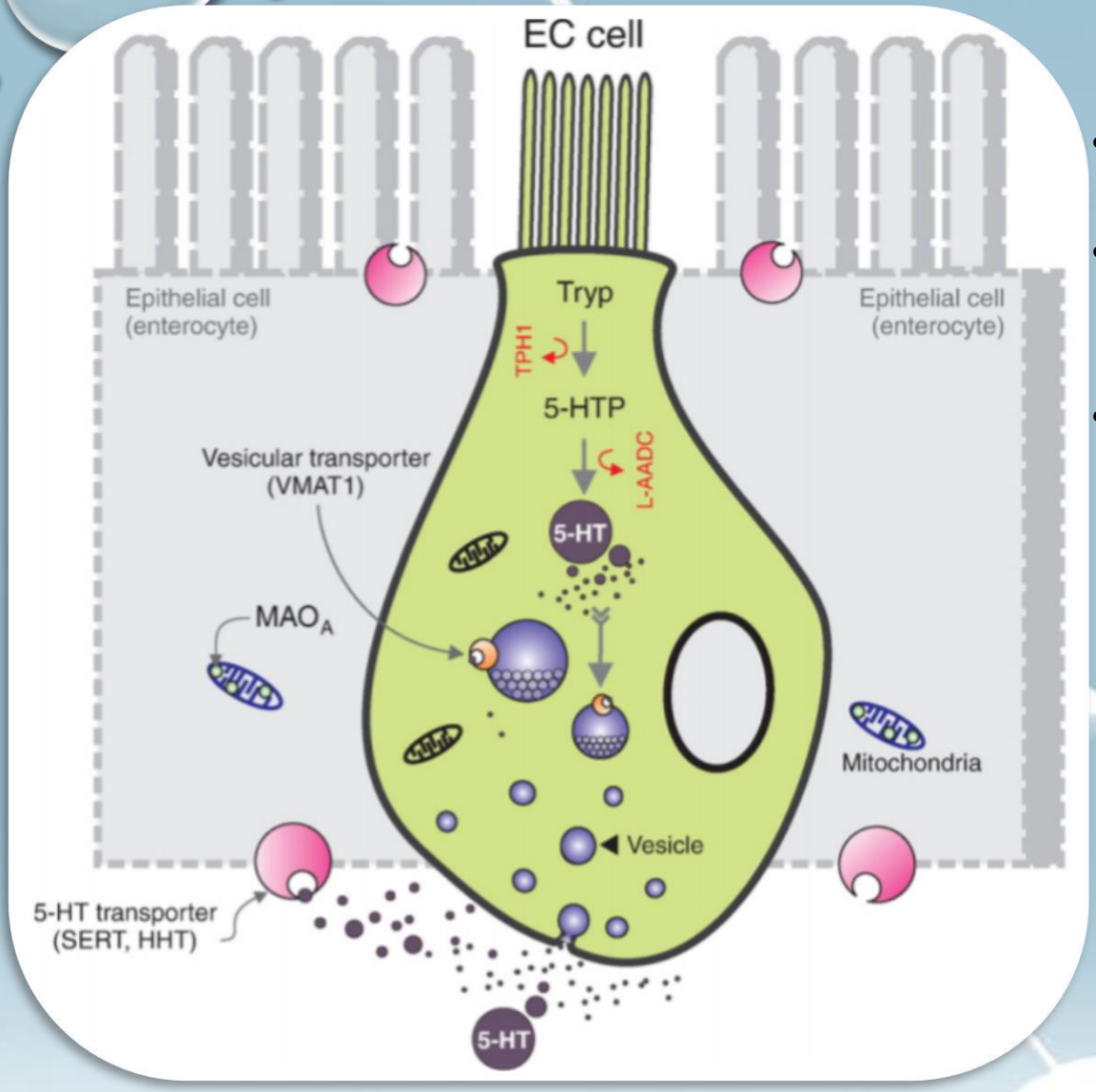
ABSTRACT

The afferent innervation of the gastrointestinal (GI) tract consists of intrinsic and extrinsic sensory neurons that respond to nutrients, chemicals or mechanical stimuli within the gut lumen. Most stimuli do not interact directly with the afferent nerves but instead activate specialised cells in the epithelium in a process of sensory transduction. It is thought that one of the first steps in this process is the release of serotonin (5-HT) from the enterochromaffin (EC) cells. The EC cells are a sub-type of enteroendocrine (EE) cells which are found among the enterocytes of the intestinal epithelium. The EC cells are responsible for the production and storage of the largest pool of 5 HT in the body. Released 5-HT can act on the intrinsic nerves and vagal endings. This review will focus on the role of 5-HT in sensory transduction and examine how the EC cell produces and releases 5-HT. We will explore recent developments that have helped to elucidate some of the proteins that allow EC cells to sense the luminal environment. Finally, we will highlight some of the findings from new studies using electrochemical techniques which allow the real-time recording of 5-HT concentrations near to the EC cell.

- Enterochromaffin cells(EC)
- Production and storage of the largest pool of 5-HT in the body
- 5-HT released from the EC cells modulates a large number of GI reflexes



Epithelium (EPI)
Submucosal plexus (SMP)
Circular muscle (CM)
Myenteric plexus (MP)
Longitudinal muscle (LM)



- A diagram of a single EC cell
- 5-HT is released mainly from the granules stored near the basal
- Granules near the apical membrane

Vesicular Monoamine Transporter 1 (VMAT1)

- diarrhoea associated with cholera
- the nausea due to chemo-or radiation therapy
- flushing and heart palpitations associated with carcinoid tumours

Goes up or Goes down?!

IBS
- increase in mucosal 5-HT turnover in post-infectious IBS
- no change in the number of EC cells count

Cell

Article

Indigenous Bacteria from the Gut Microbiota Regulate Host Serotonin Biosynthesis

Jessica M. Yano,[1] Kristie Yu,[1] Gregory P. Donaldson,[1] Gauri G. Shastri,[1] Phoebe Ann,[1] Liang Ma,[2] Cathryn R. Nagler,[3] Rustem F. Ismagilov,[2] Sarkis K. Mazmanian,[1] and Elaine Y. Hsiao[1,*]

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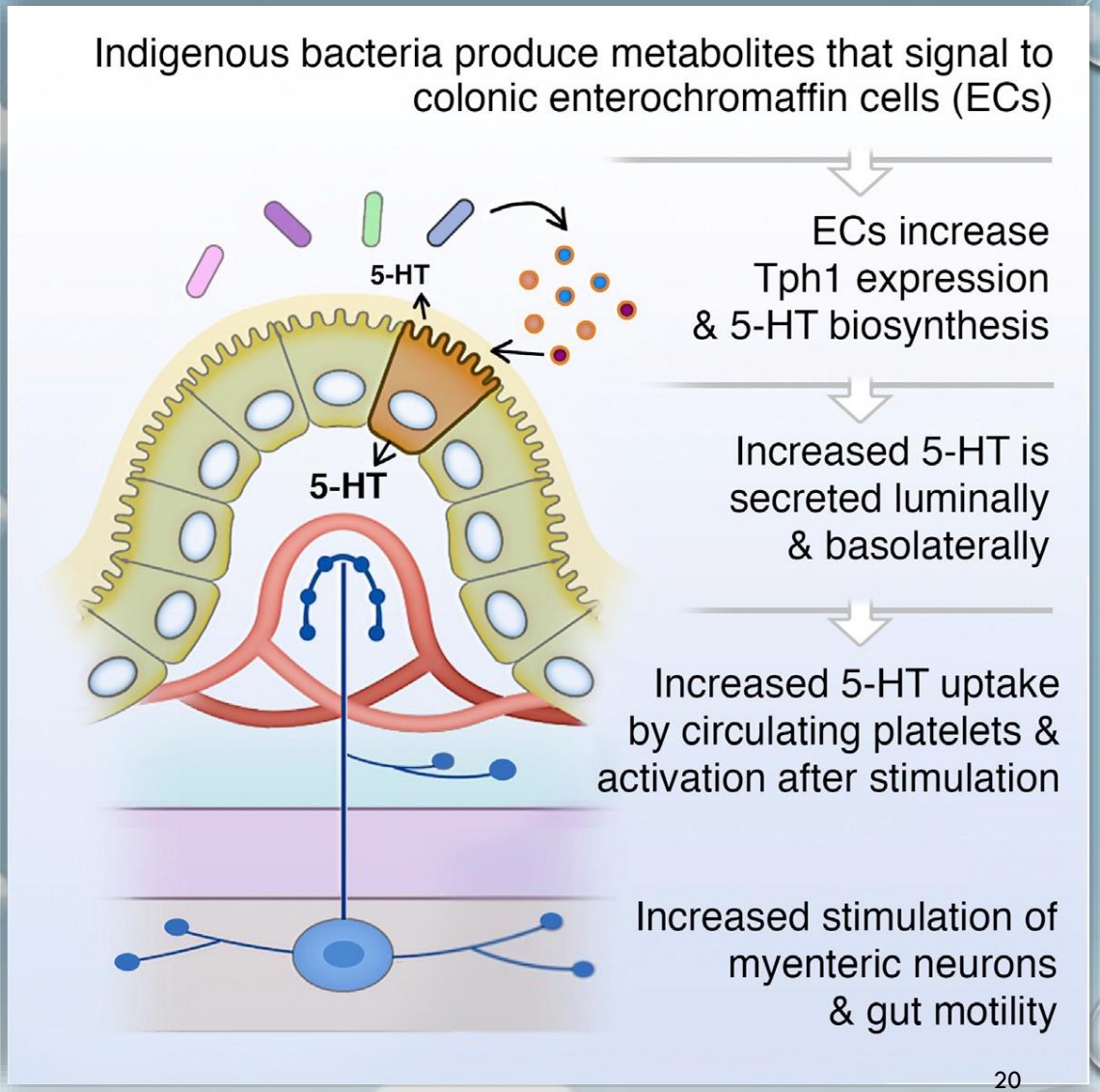
http://dx.doi.org/10.1016/j.cell.2015.02.047

- ✓ Regulate 5-HT in colon and blood
- ✓ Improve 5-HT-related disease symptoms

- ✓ Spore-forming microbes (Sp)
- ✓ Bacillus species
- ✓ Clostridium species

- ✓ Specific Pathogen-Free (SPF)
- ✓ Germ-Free (GF)



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- ✓ Paul P. Bertrand, Serotonin release and uptake in the gastrointestinal tract. 2010

Thank You !