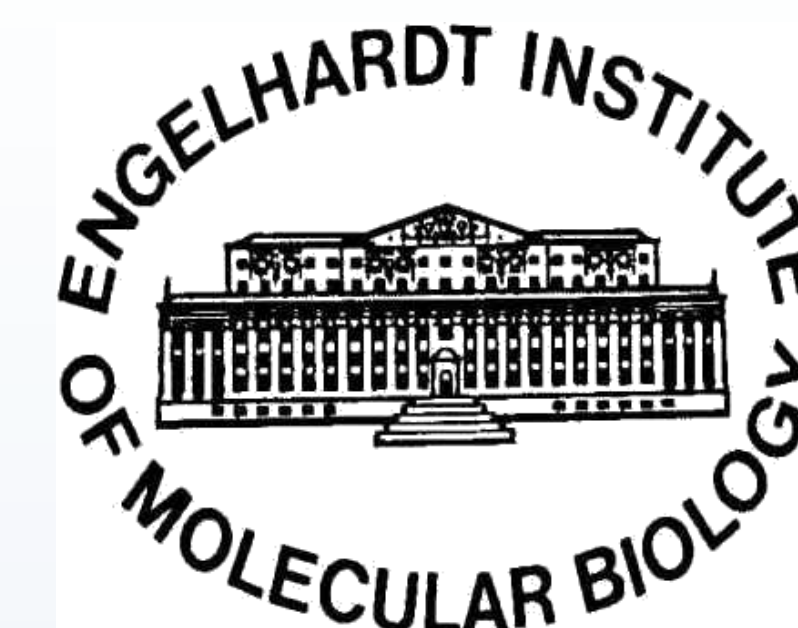




BIOGENIC AMINES IN THE HEALTH CHALLENGE CAUSED BY THE CHANGING ARCTIC CLIMATE



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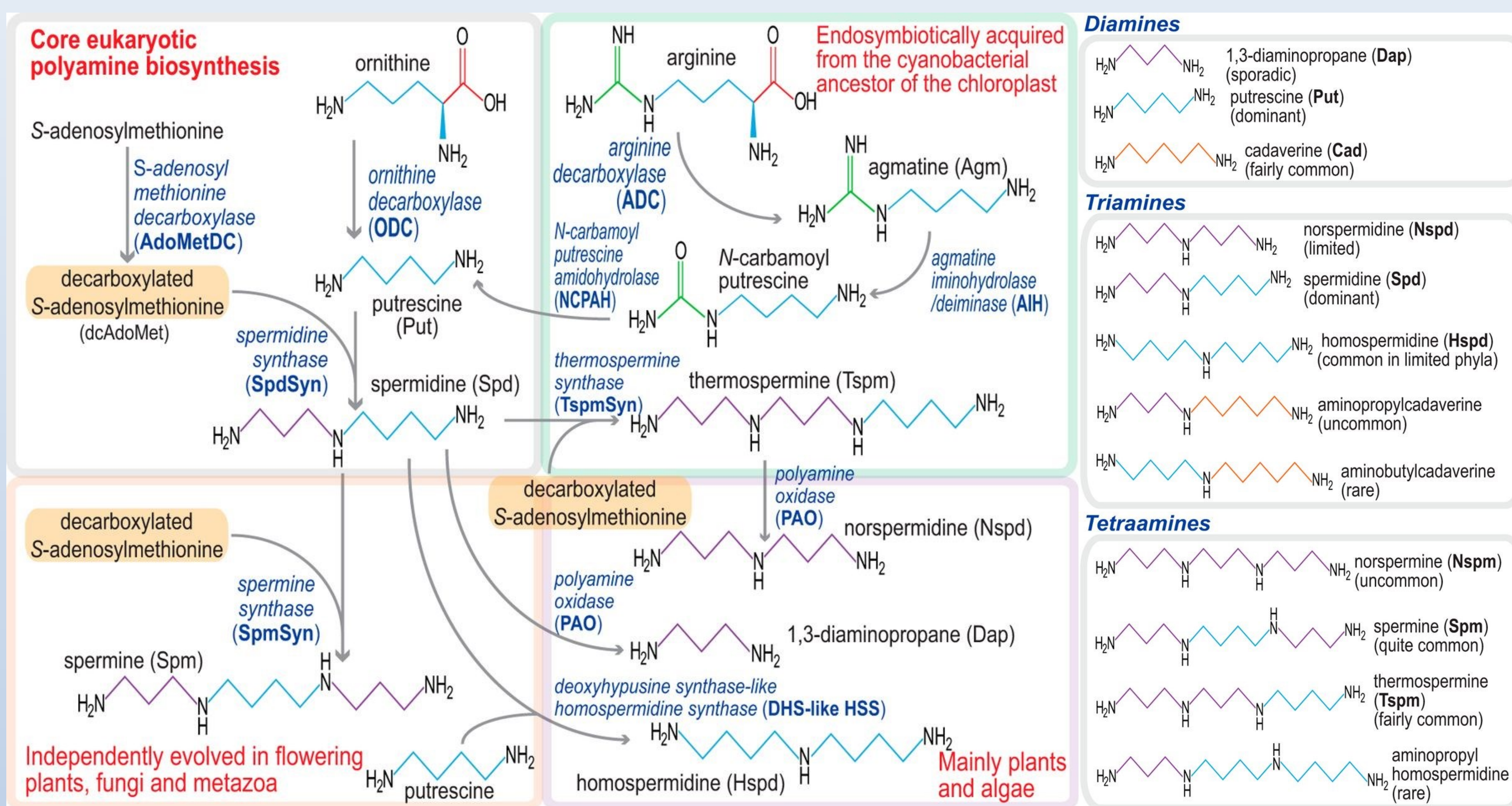
- Due to the climate change, Arctic ecosystems are challenged by new pathogens, diseases and fluctuating environmental conditions causing abiotic (i.e. temperature, drought, salinity, sunlight) and biotic (i.e. microbes, viruses, fungi, parasites) stress
- Polyamines are a class of important biogenic amines, acting as universal molecules protecting against abiotic and biotic stress
- Polyamine metabolism is linked to central metabolic pathways in all three domains life
- The prevalent polyamine species as well as the polyamine metabolic enzymes and their biological properties differ between microbes, plants, parasites, fungi and mammalian cells

THE POLYAMINE SPERMIDINE

- Essential for the proliferation and differentiation of many cell types
- Protects against cardiovascular diseases
- Necessary for bacterial biofilm formation, which increases antibiotic resistance (even up to 1000-fold)

ANALYSIS PLATFORMS

- HPLC
- LC-MS/MS
- NMR
- recombinant proteins
- cell/organ cultures
- *in vivo* testing in mice
- disease models in mice



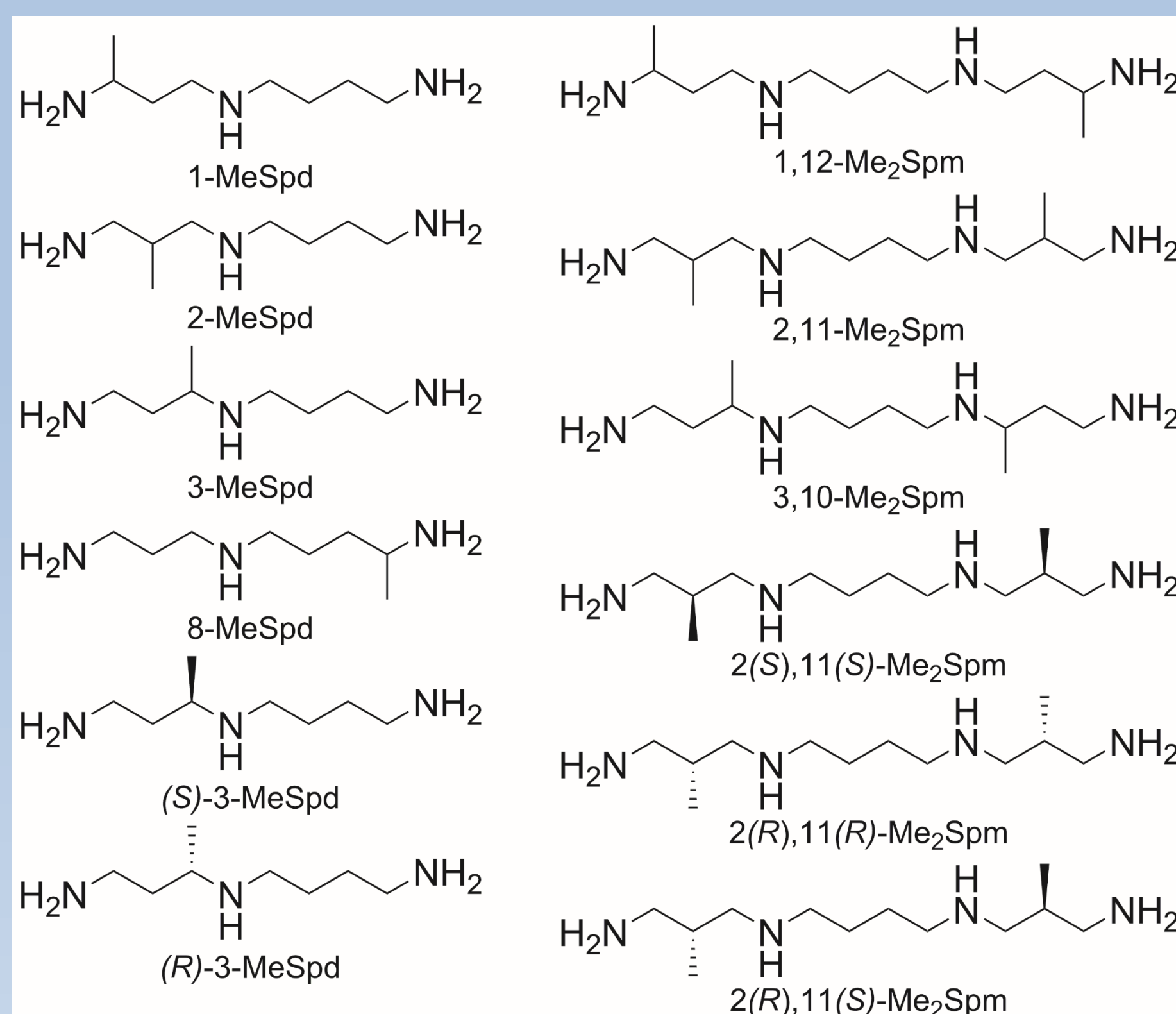
Michael AJ. Polyamines in Eukaryotes, Bacteria, and Archaea. J Biol Chem. 2016 Jul 15;291(29):14896-903.

AIMS OF THE PROJECT

- To find differences in polyamine metabolism between host and microbe, healthy and diseased cell
- To synthesize novel polyamine analogs in order to develop therapeutics for human/animal/plant diseases associated with the changing Arctic climate

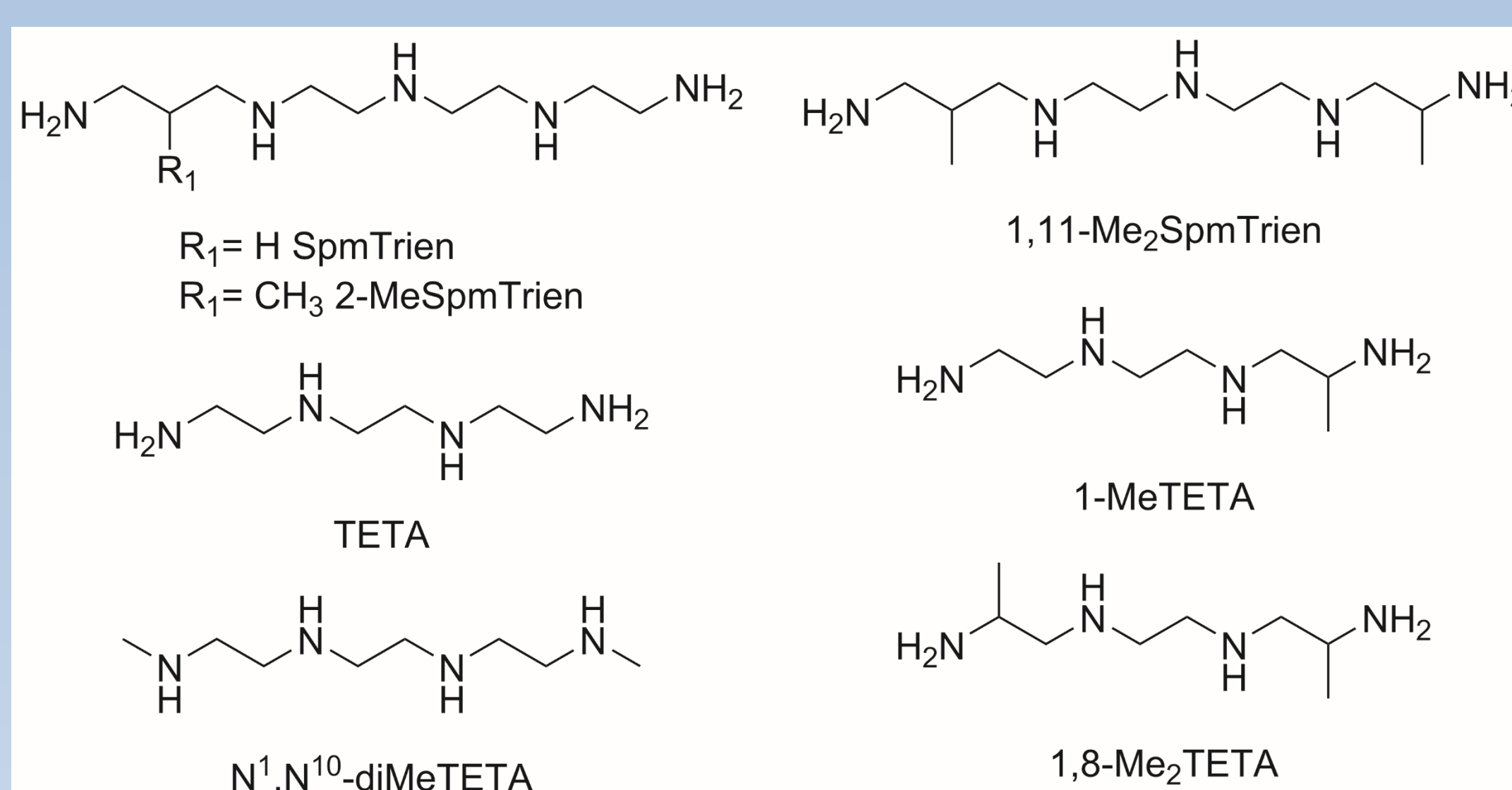
C-METHYLATED ANALOGS

- Modifying the biological properties of polyamine analog by changing the position of methyl group and its stereoconfiguration



CHARGE-DEFICIENT ISOSTERIC ANALOGS

- TETA, spermidine analog and Cu^{2+} chelator, is used as a drug for Wilson's disease, but it has also shown to alleviate diabetes-associated end-organ diseases and act as anti-cancer agent
- TETA has low bioavailability and fast metabolism \Rightarrow development of more stable analogs and precursors with higher bioavailability



AMINO-OXY ANALOGS

- Inhibitors of polyamine biosynthetic enzymes – difference between mammalian vs microbial enzymes
- Targeted enzymes and metabolic pathway include arginine decarboxylase and trypanothione pathway

