Enzyme review

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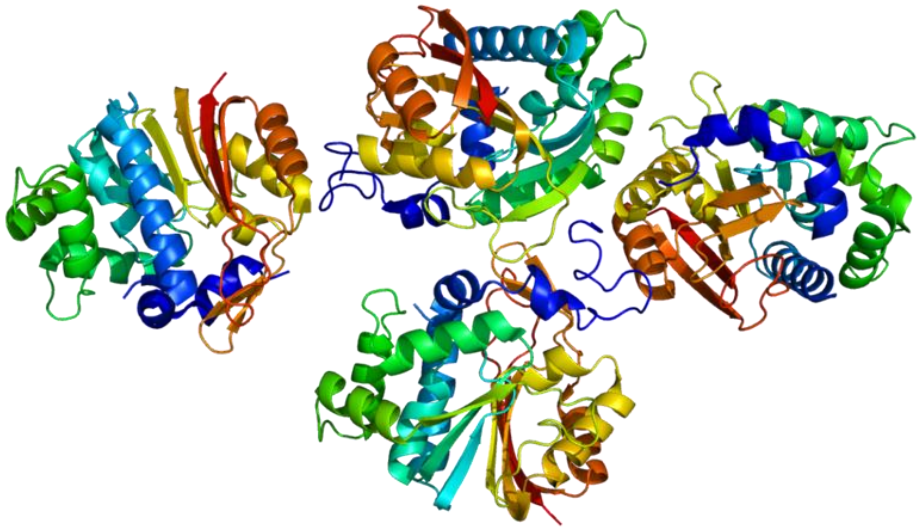
Common

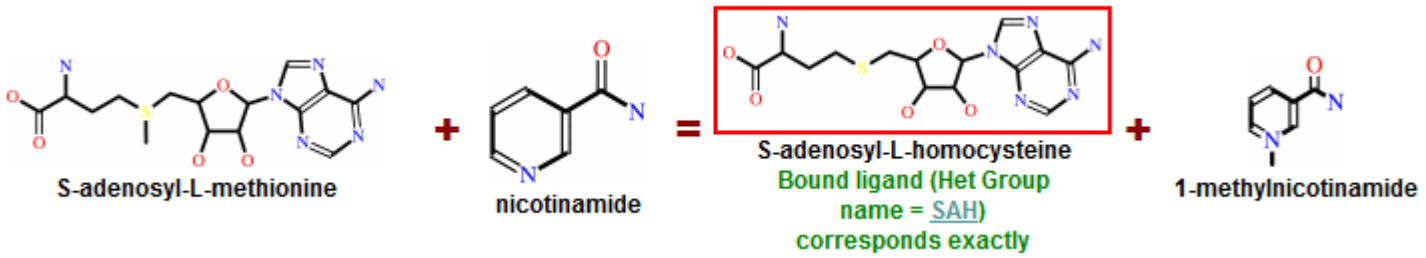
- Name: Human Nicotinamide N-methyltransferase (NNMT)
- Code: EC 2.1.1.1
- Organism: Homo Sapiens
- Classification: transferase
- Structural weight: 127402,23
- Sequence status: complete.



Annotation

- Catalyzes the N-methylation of nicotinamide and other pyridines to form pyridinium ions. This activity is important for biotransformation of many drugs and xenobiotic compounds.
- Catalytic activity:

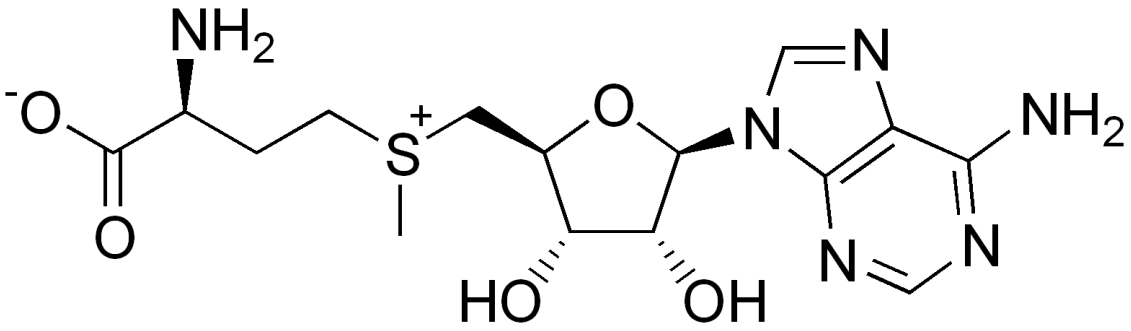
S-adenosyl-L-methionine + nicotinamide = S-adenosyl-L-homocysteine + 1-methylnicotinamide



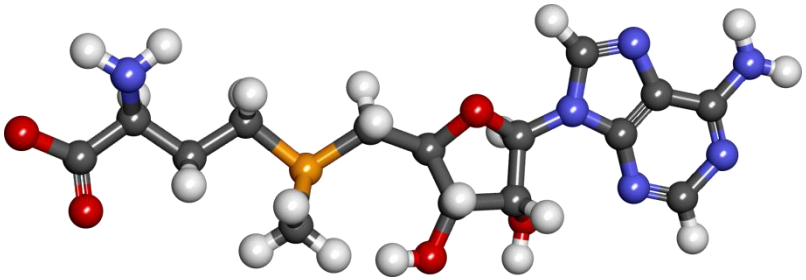
Pic 1 – Graphic reaction

Substrates

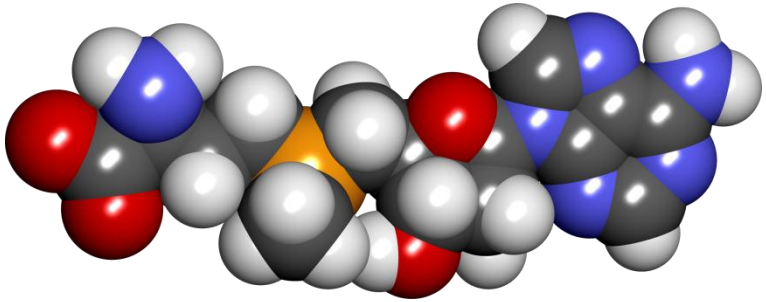
***S*-Adenosyl methionine** is a common cosubstrate involved in methyl group transfers.



Pic 2 – Strucrure of *S*-Adenosyl methionine



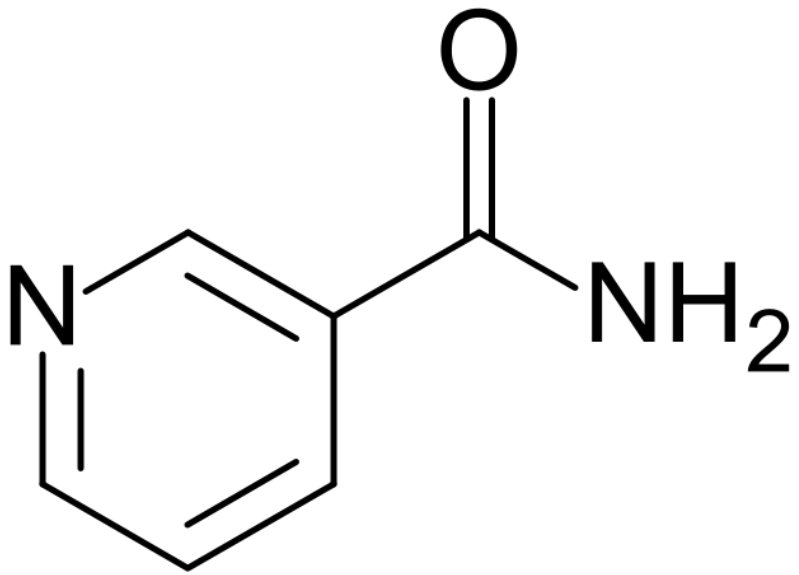
Pic 3 – A ball-and-stick diagram of S-adenosyl methionine



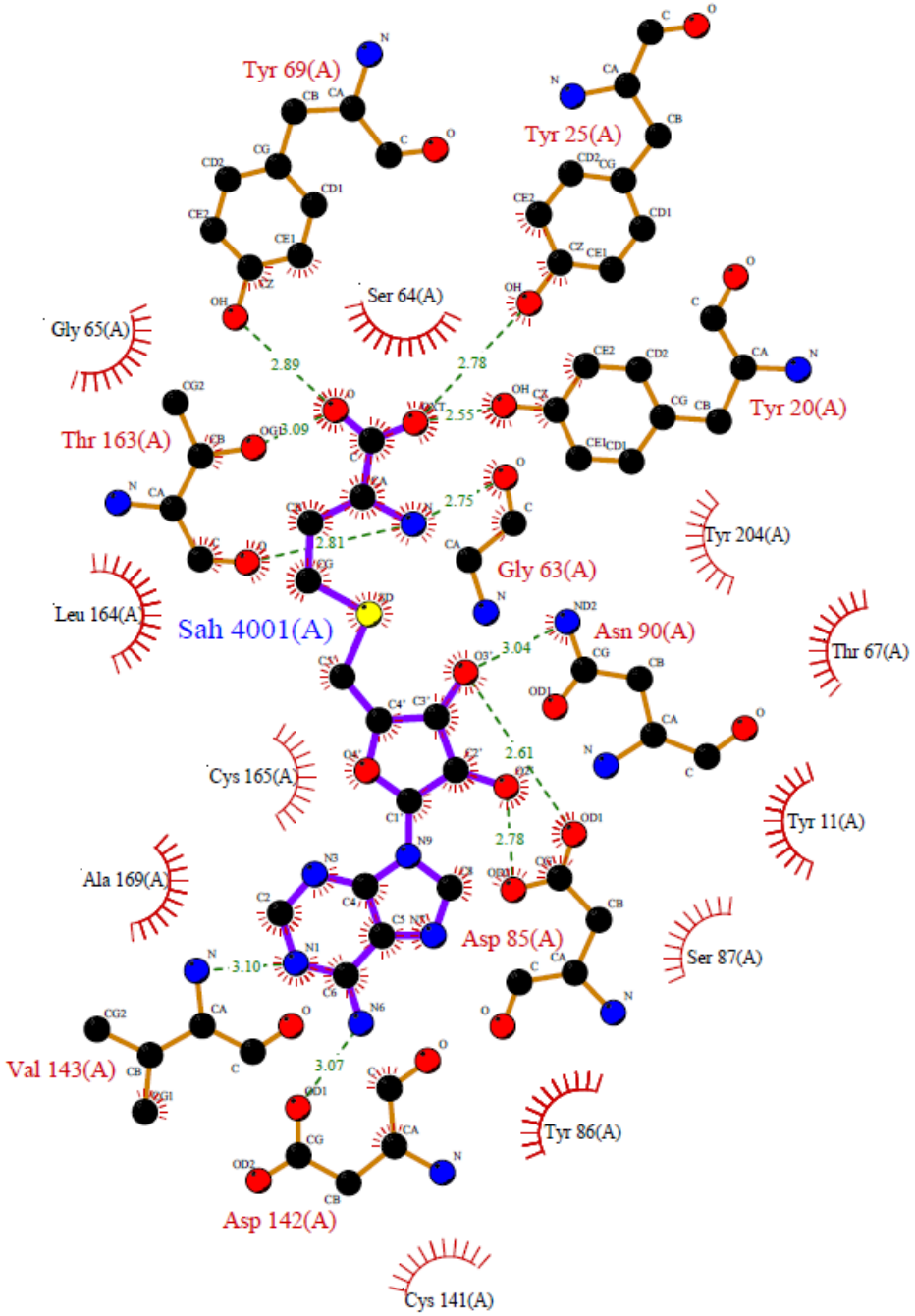
Pic 4 – A space filling diagram of S-adenosyl methionine

Substrates

Nicotinamide, also known as niacinamide and nicotinic acid amide, is the amide of nicotinic acid (vitamin B_3 / niacin).

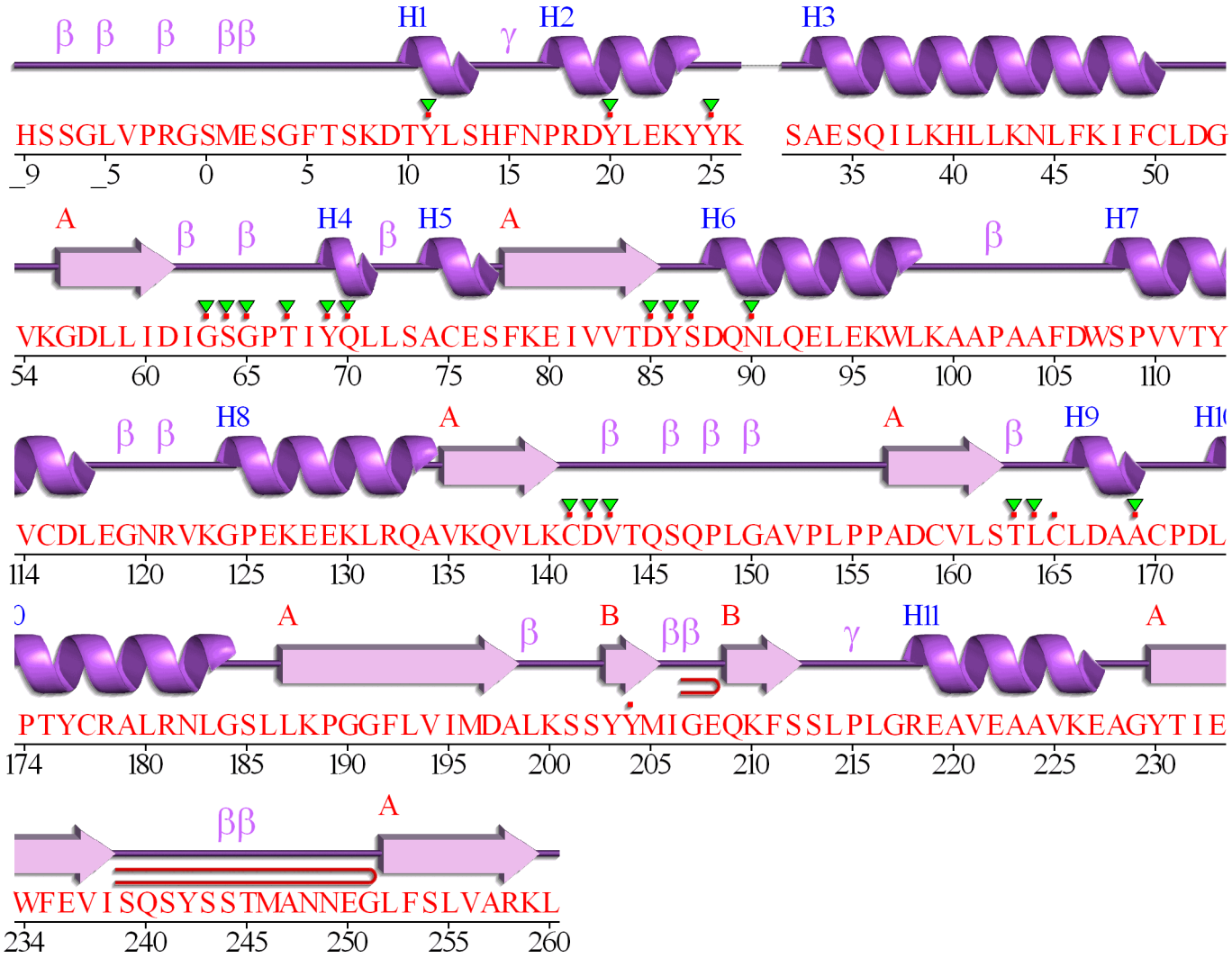


Pic 5 – Chemical structure of nicotinamide.



Pic 6 – LIGPLOT of interactions involving ligand

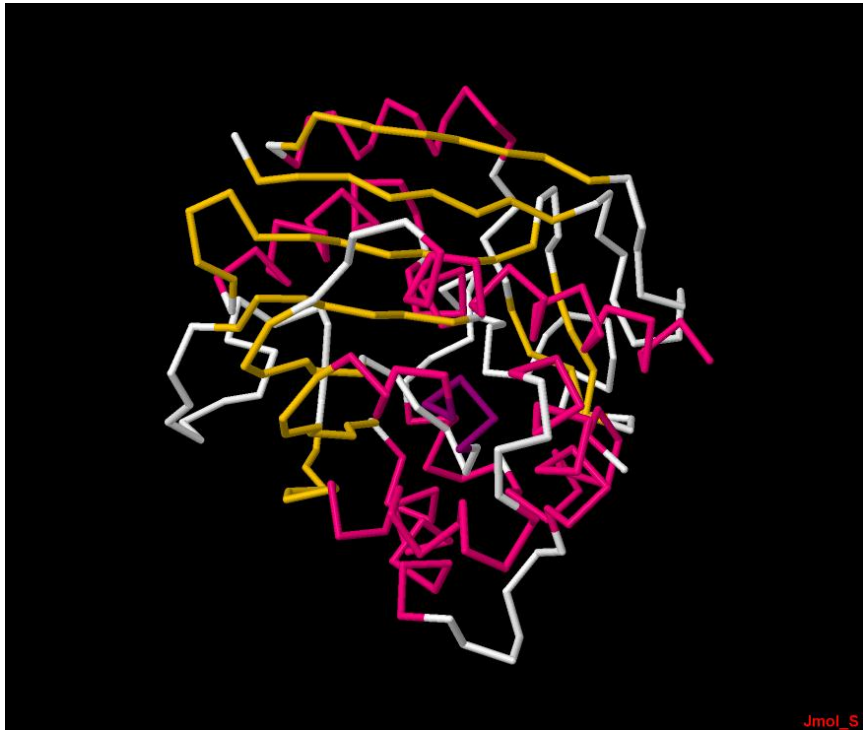
Structure of NNMT



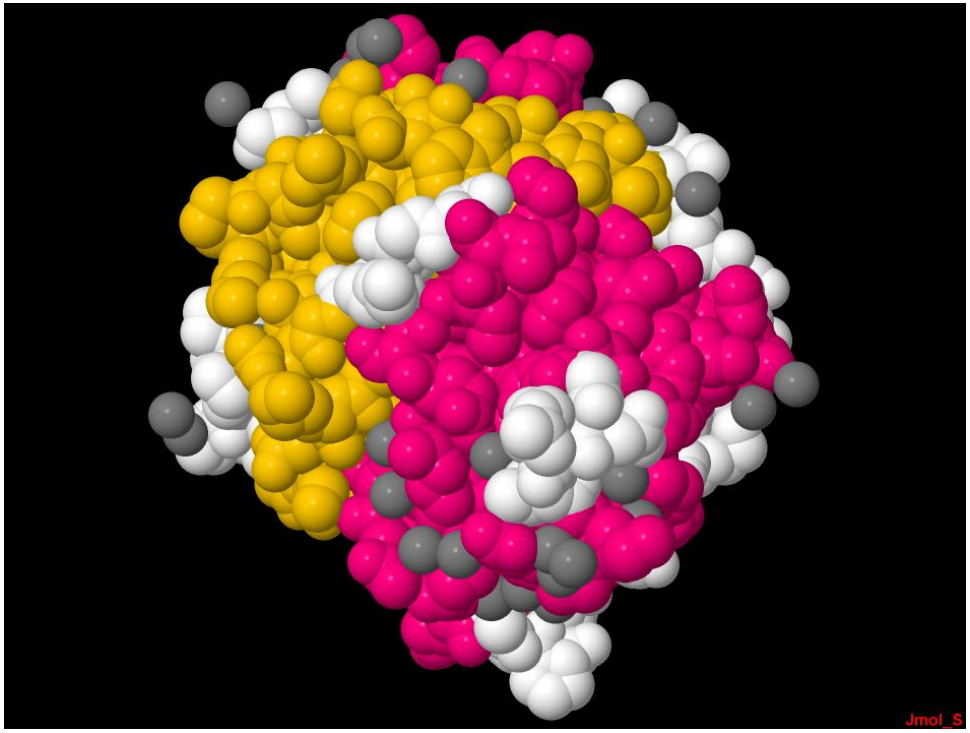
Pic 7 – Secondary structure

Structure of NNMT

Pic 8 – Globular structure of NNMT



Pic 9 – A skeleton diagram of NNMT



Pic 10 – A space filling diagram of NNMT

Is it useful?

- **Disease relevance of NNMT:**
  - Cotransfection of a HNF-1beta expression plasmid increased NNMT promoter activity significantly in both HNF-1beta-positive and -negative thyroid cancer cell lines and Hep G2 liver cancer cells [1].
  - Human liver NNMT activity has a bimodal frequency distribution, an observation which raises the possibility that this enzyme activity might be regulated by a genetic polymorphism, a polymorphism that could have functional implications for individual differences in drug and xenobiotic toxicity [2].
  - CONCLUSIONS: It is proposed that NNMT serum levels may have significance in the early detection and in the management of patients with colorectal cancer [3].
  - NNMT has been proposed as a link between the environmental and genetic factors of Parkinson disease (PD) [4].

- **Analytical, diagnostic and therapeutic context of NNMT**
  - After Northern blot analysis confirmed that NNMT is highly expressed in the liver, eight human hepatic biopsy samples, four each with 'low' or 'high' levels of activity, were used to perform quantitative Western blot analysis [5].
  - In an attempt to develop an experimental animal model for pharmacogenetic studies of NNMT, we determined optimal conditions for the measurement of hepatic NNMT activity in C57BL/6J mice [6].
  - We report the characterisation of the hepatic NNMT activity in cytosol from normal human livers, enzyme protein levels determined by Western blotting and ELISA and mRNA levels determined by SDS-PAGE/Northern blotting [7].

Methods

- PCR;
- Amplification;
- Cloning;
- Two-dimensional gel electrophoresis;
- Mass spectrometry;
- NNMT antibodies;
- Northern, western blot analysis;
- ELISA.

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2004	2

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Top Terms	Publications
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Nicotinamide N-Methyltransferase	88
Nicotinamide N-methyltransferase	71
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Methyltransferases	42
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catalytic activity	24
Enzyme Activation	23
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Up-Regulation	22
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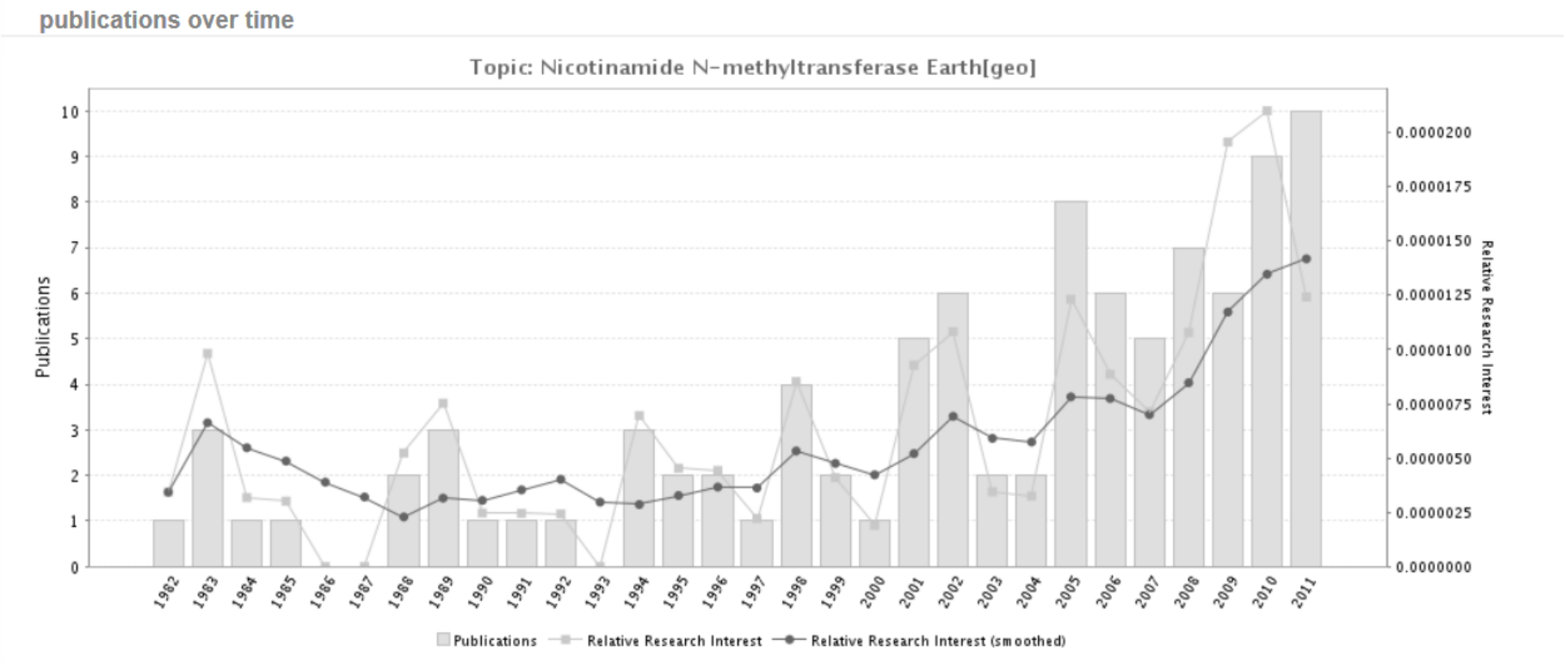
metabolic process	21
methylation	21

Publications



Pic 11 – Publications from Gopubmed

World map

Pic 12 – Worldmap from Gopubmed

References

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5. **Human nicotinamide N-methyltransferase pharmacogenetics: gene sequence analysis and promoter characterization.** Yan, L., Otterness, D.M., Weinshilboum, R.M. *Pharmacogenetics* (1999)
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7. **A direct correlation between nicotinamide N-methyltransferase activity and protein levels in human liver cytosol.** Smith, M.L., Burnett, D., Bennett, P., Waring, R.H., Brown, H.M., Williams, A.C., Ramsden, D.B. *Biochim. Biophys. Acta* (1998)

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