

***“Essentiality of PZA” Workshop***  
***organized by the Working group on new TB***  
***drugs***

**Under the chairmanship of**

- William Bishai-WB (co-chair)
- Melvin Spigelman-MS (co-chair)

**Took place on June 1, 2011 at**  
**NIH/NIAID | 6610 Rockledge Drive, Room**  
**4008 | Bethesda, Maryland**

# Objectives and participants

## **Objectives:**

- Discuss critical issues surrounding the essentiality of PZA in TB treatment
- Develop suggestions for future research projects
- Foster collaboration among participating groups

## **Participants:**

- invitation only workshop
- small group of approximately 25 individuals with diverse scientific backgrounds from the public and private sectors in an effort to stimulate productive discussion
- Moderator: John Blanchard
- Cherise Scott, Secretariat

# Main issues addressed by the workshop

1. Mechanism(s) of action including the potential target, the range of susceptible organisms, the role of acidic environment, immune-modulator effect (leishmania)

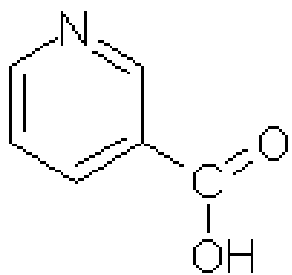
## **Pyrazinamide Inhibits Trans-Translation in *Mycobacterium tuberculosis***

Wanliang Shi, Xuelian Zhang, Xin Jiang, Haiming Yuan, Jong Seok Lee, Clifton E. Barry, 3rd, Honghai Wang, Wenhong Zhang, Ying Zhang

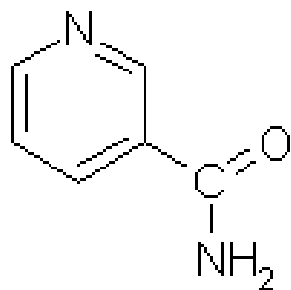
Scienceexpress.org / August 11 2011 / Page 1 /  
10.1126/science.1208813

# Main issues addressed by the workshop

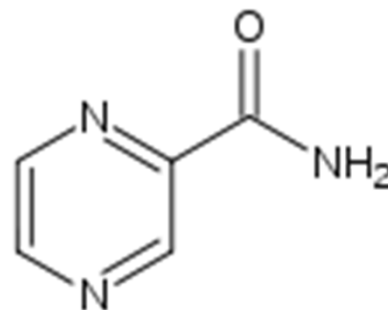
2. The past and new analogues of PZA: Why does the addition of a nitrogen atom in the pyridine ring increase by ~ 7 times the antituberculosis activity of nicotinamide? Is nicotinamide, like pyrazinamide, synergistic with rifampin?



Nicotinic Acid



Nicotinamide



**Pyrazinamide**  
(pyrazine-2-carboxamide)

# Main issues addressed by the workshop

3. Drug susceptibility test: from phenotypic to genotypic tests? From not possible to be performed on routine basis to “automated” test?
4. Timing of PZA use : why is such a unique sterilizing drug used during the initial (bactericidal) phase, only during the initial phase, and not in the continuation (sterilizing) phase of treatment for tuberculosis?

# Conclusions

- Fascinating presentations
- Active discussions
- Strong motivation to further investigate the mechanisms of PZA activity
- How to translate into concrete collaborations?