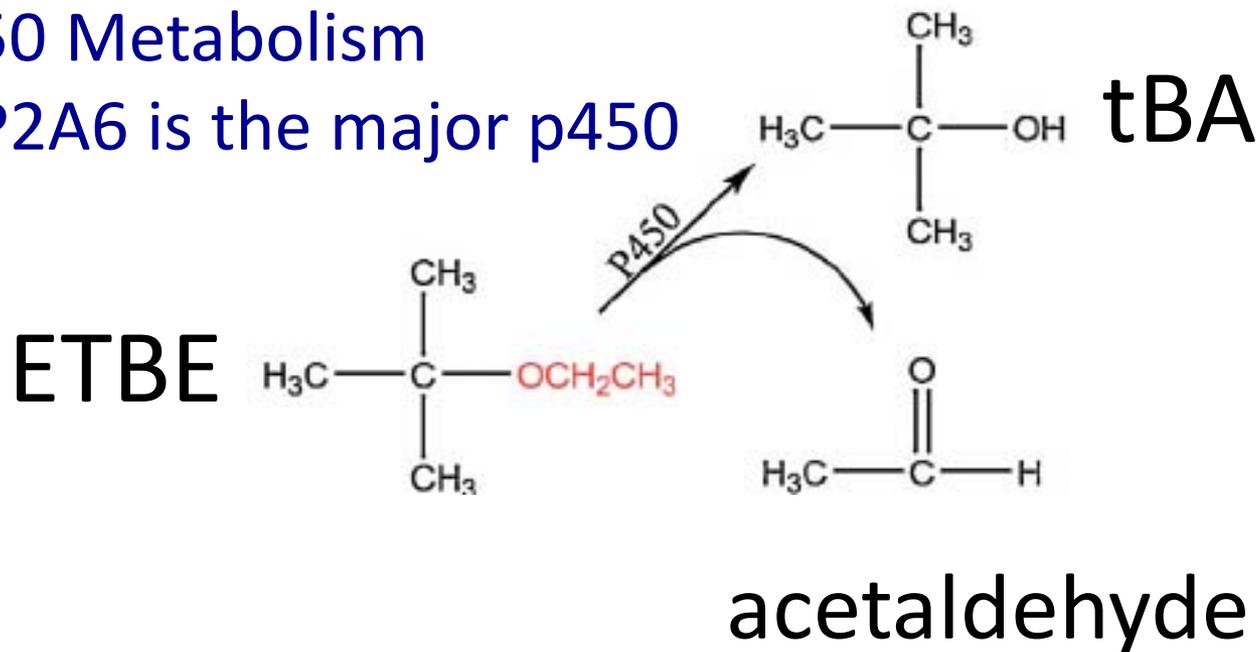


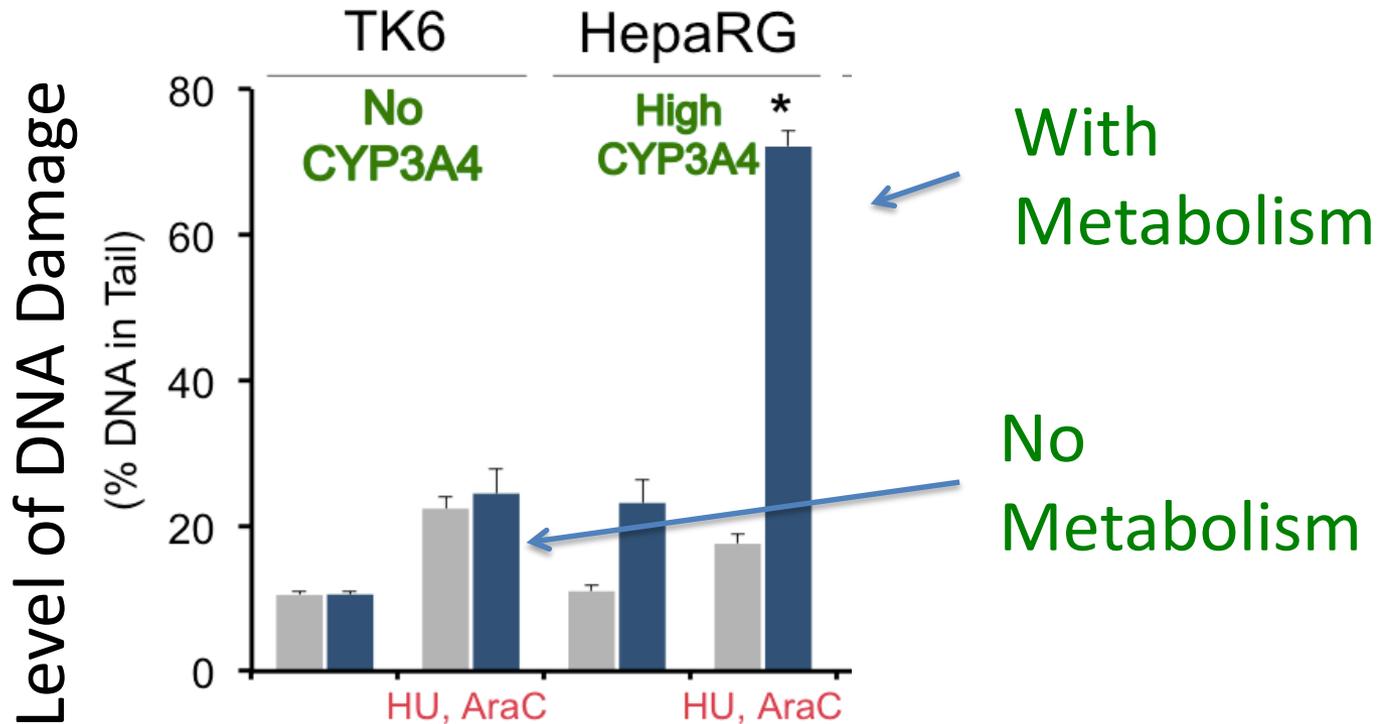
NOTICE: **Do Not Cite or Quote.** Preliminary Comments submitted by individual members are for review and to assist meeting deliberations by the CAAC-ETBE/tBA committee. These comments do not reflect consensus advice or recommendations, and have not been reviewed or approved by the chartered SAB and do not represent EPA policy.

Preliminary Comments from Dr. Bevin Engelward  
August 16, 2017

P450 Metabolism  
CYP2A6 is the major p450



## DNA Damaging Agents can Depend on Metabolism: Example of Aflatoxin

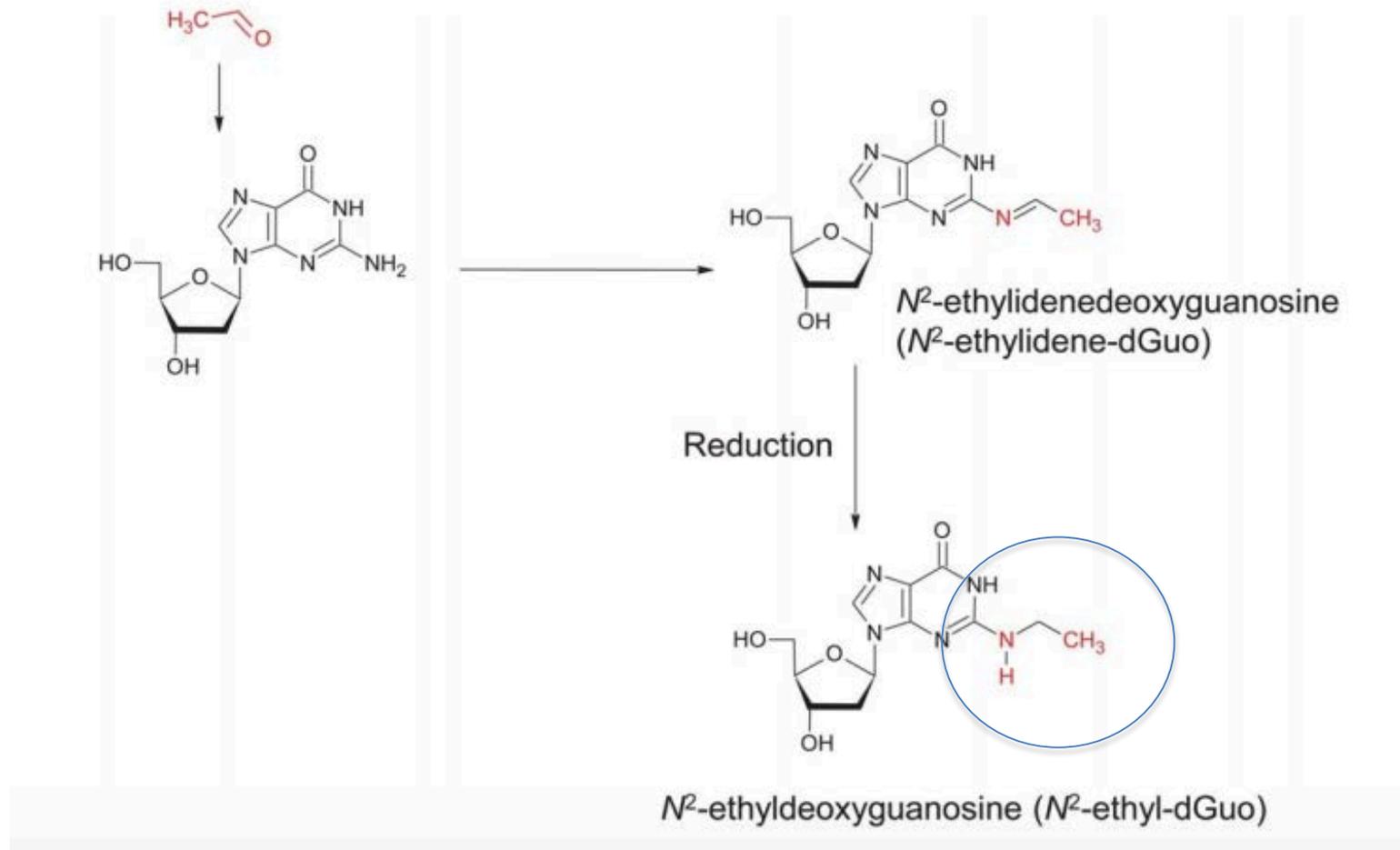


$n \geq 3$

Error bars = SEM

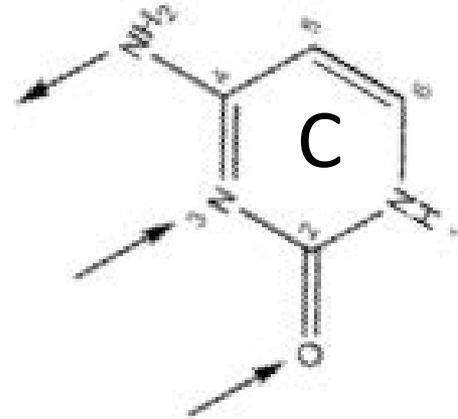
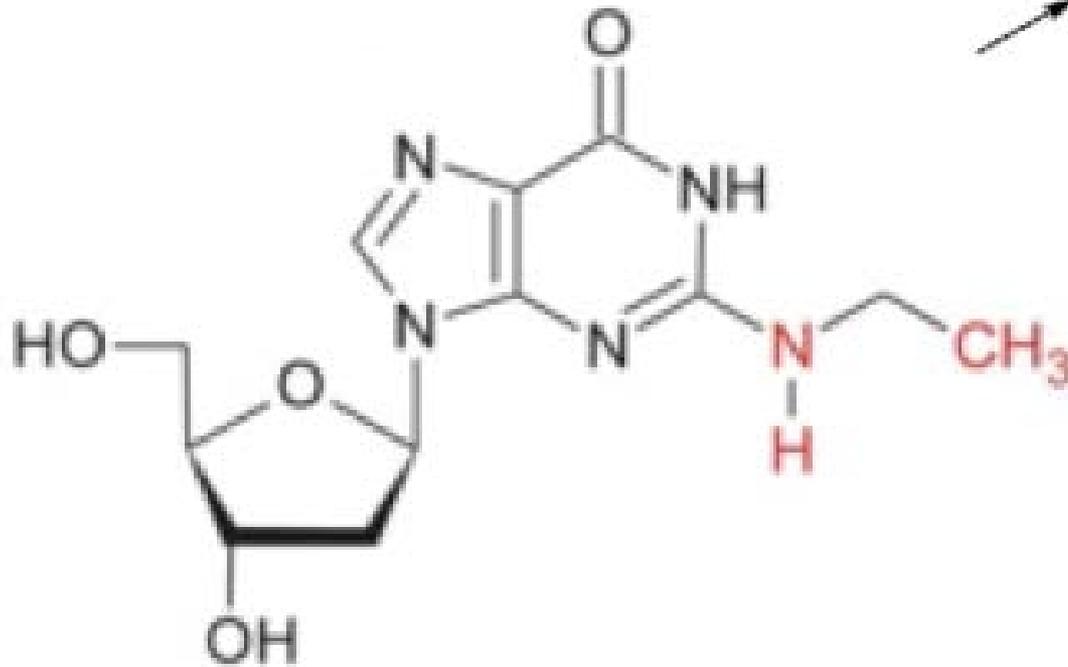
\* $p < 0.05$ , Student's t-test, 2-tailed, paired

# Acetaldehyde Can Directly React with DNA to Damage Bases

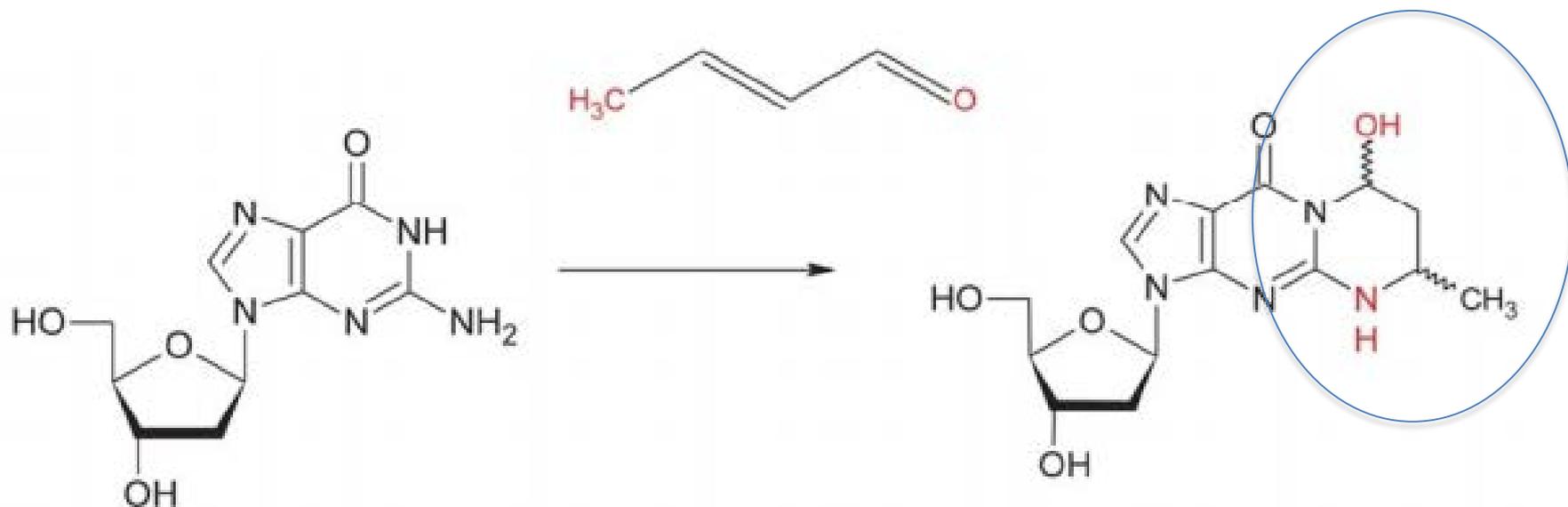


# Acetaldehyde-induced damage disrupts base pairing

*N*<sup>2</sup>-ethyldeoxyguanosine

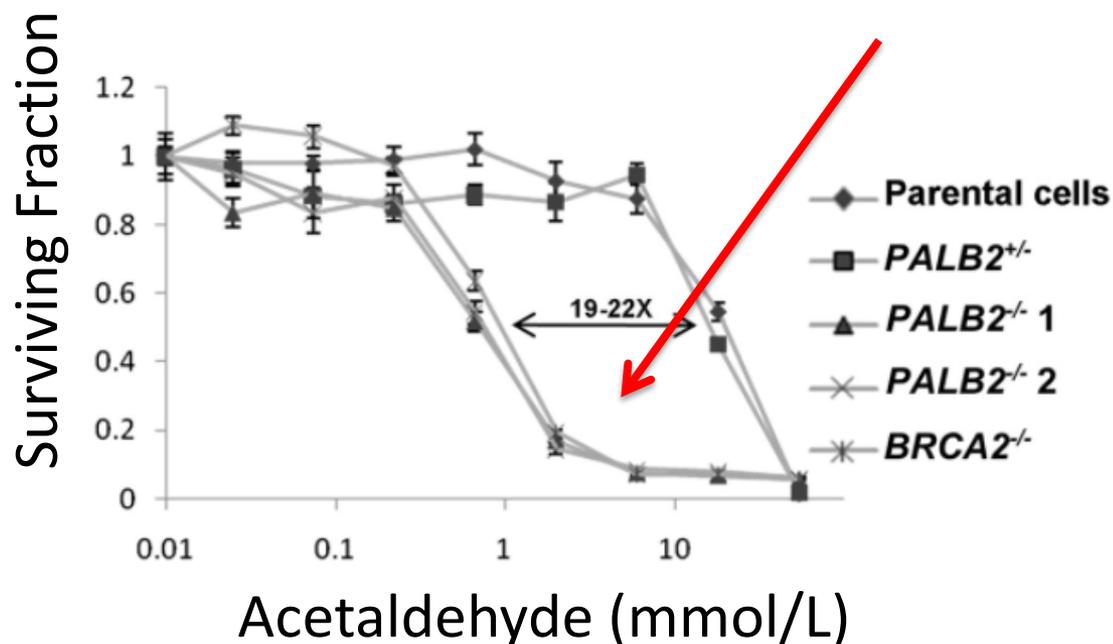


## Crotonaldehyde, formed by two acetaldehydes, can also damage DNA

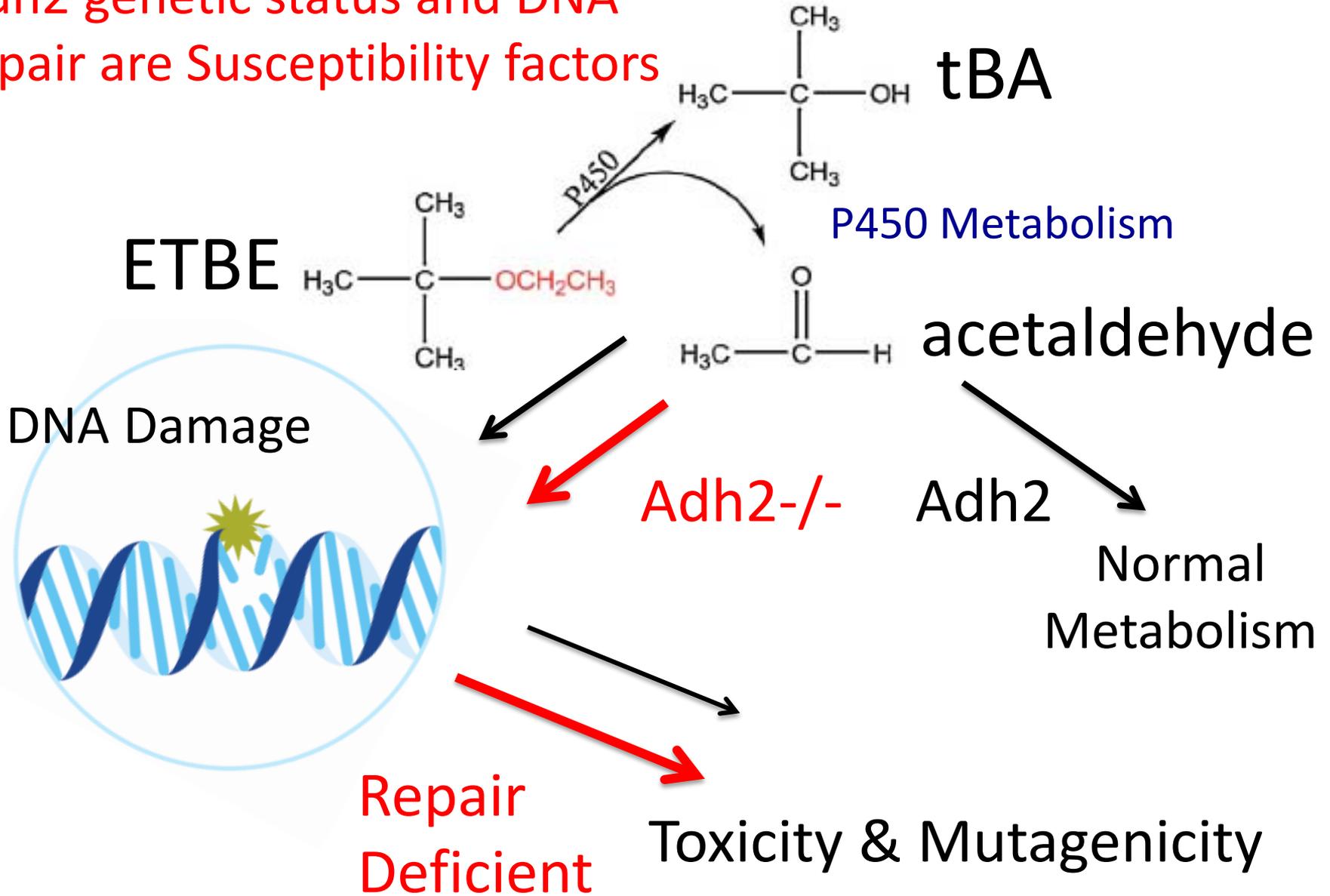


# DNA Repair is a Susceptibility Factor

Cells Deficient in DNA Repair  
are Sensitive to Acetaldehyde



# Adh2 genetic status and DNA repair are Susceptibility factors



## Acetaldehyde Levels Assume ETBE = Acetaldehyde

Steady state in people is  $\sim 50 \text{ uM}^*$

Human Exposure: Beer is  $\sim 100 \text{ uM}$

Rats were  $10,000 \text{ uM}$  ( $1000 \text{ mg/kg}$ )

(One water estimate in NIAIST was  $1110 \text{ uM}^{**}$  )

Acetaldehyde in People Steady State:

\*Schuckit and Raysee, Science 283, 54 (1979)

\*Korsten, New England Journal of Medicine, 292, 386 (1975)

\*\*Based on well water, national assessment; page 58.

March 21, 2008

Research Center for Chemical Risk Management  
National Institute of Advanced Industrial Science and  
Technology

**NIAIST  
STUDY**

## **ETBE in Air**

### Environment

**Highest listed in the document: 38 ug/m<sup>3</sup> (NIAIST Table 1-9)**

### Rats

**20,000 mg/m<sup>3</sup> some studies (Saito 2013; IRIS page 1-10)**

### Comparison

**Equals 20,000,000 ug/m<sup>3</sup>**

**20 million versus 38 =**

**~500,000 fold higher in experiment compared to 'real world' estimate.**

#### Location of funded research

The Research Center for Chemical Risk Management, National Institute of Advanced Industrial Science and Technology (Tsukuba West), 16-1 Onogawa, Tsukuba city, Ibaraki Prefecture, 305-8569 Japan