



TA-CD – the anti-cocaine vaccine

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Summary

- **Cocaine addiction is a serious problem in the US and EU.**
- **There are currently no pharmacotherapies to help addicts to quit**
- **TA-CD is a novel approach to treatment, targeting cocaine in circulation**
- **Proof of concept established in preclinical studies**
- **Phase I and II studies have shown**
 - **vaccine is safe and well tolerated**
 - **promising indications of efficacy**
- **Phase IIb study (132 patients, randomised, placebo-controlled) is due to report June 2006**

**Vaccine may
help addicts
kick the habit**

**Vaccine could
end drug abuse**

**Vaccine helps smokers
and cocaine users to quit**

Vaccine could end drug addiction

**Anti-addiction
vaccine offers
hope to quitters**

**JAG TO STOP
ADDICT KIDS**

Cocaine Addiction – the problem

- **US**
 - **2m regular cocaine users in US¹**
 - **25% Americans between ages 26-34 used cocaine²**
 - **33.9m Americans age >12 reported lifetime use of cocaine³**
 - **500,000 emergency hospital visits annually²**
- **EU**
 - **Up to 10% lifetime prevalence in 15-34 age group⁴**
 - **4% recent prevalence in UK and Spain⁴**



¹ Office of Applied Studies, 2002 National Survey on Drug Use and Health

² Drug-Rehab.org

³ NIDA, figures for 2002

⁴EMCDDA, 2004

The A-Z (almost!) of cocaine treatment so far

amantadine

cabergoline

disulfiram

fluoxetine

baclofen

effexor

GVG

isradipine

Java

modafinil

Help!

ketoconazole

ondansetron

naltrexone

pergolide

lamotragine

sertraline

quitiapine

risperdol

UC2Jokes

venlafaxine

tiagabine

w x y z to follow!



Features of cocaine addiction

- **Addiction is a chronic relapsing disorder**
- **When cocaine is taken, it is transported rapidly to the brain**
- **Speed of transport depends on how cocaine is taken**
- **It is the quantity and speed of delivery of cocaine into the brain that is important in generating the high**
- **“Priming” is associated with this effect, often leading to binging**

A strategy for cracking cocaine addiction

- **Addiction is a chronic relapsing disorder**
- **It is very unlikely that an addict will quit unless highly motivated**
- **It is expected that a patient will lapse during treatment**
- **Priming contributes to turning a lapse into a binge**
- **Priming is a function of the rate and extent of cocaine entry into the brain**
- **Blocking the priming effect can keep a lapse from becoming a full blown relapse**

Vaccination – a novel approach to cocaine addiction

- **Vaccinate the patient**
- **Patient makes antibodies**
- **Antibodies remain in circulation for several months**
- **If the patient takes cocaine, it is bound by circulating antibodies**
- **Antibody:cocaine complexes cannot cross the blood-brain barrier. The amount of cocaine reaching the brain and also the speed of delivery are thus reduced.**
- **This reduces or prevents the high and the associated priming effect**

Vaccines of Addiction - Product Concept

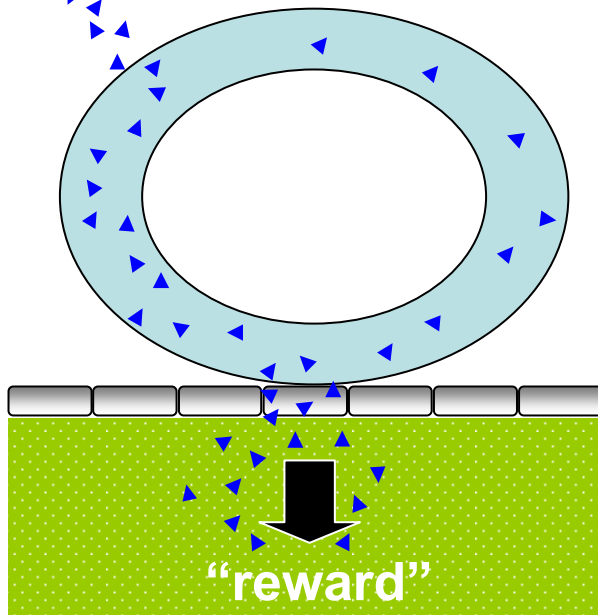
Before vaccination

After vaccination

Cocaine

Cocaine

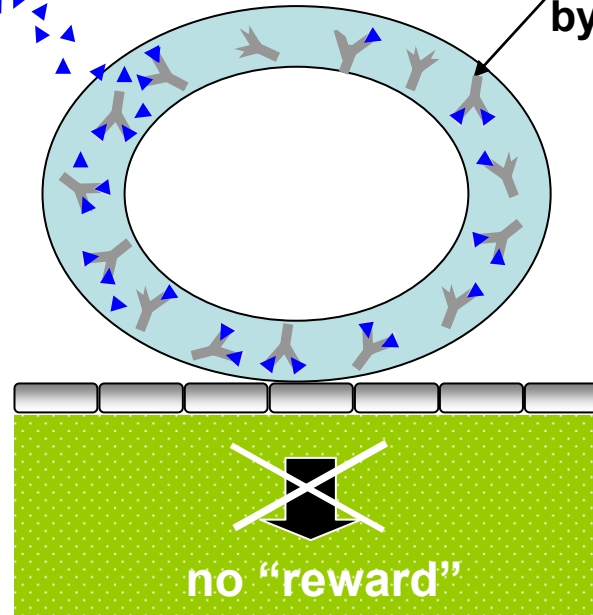
Antibodies produced by immune system



Circulation

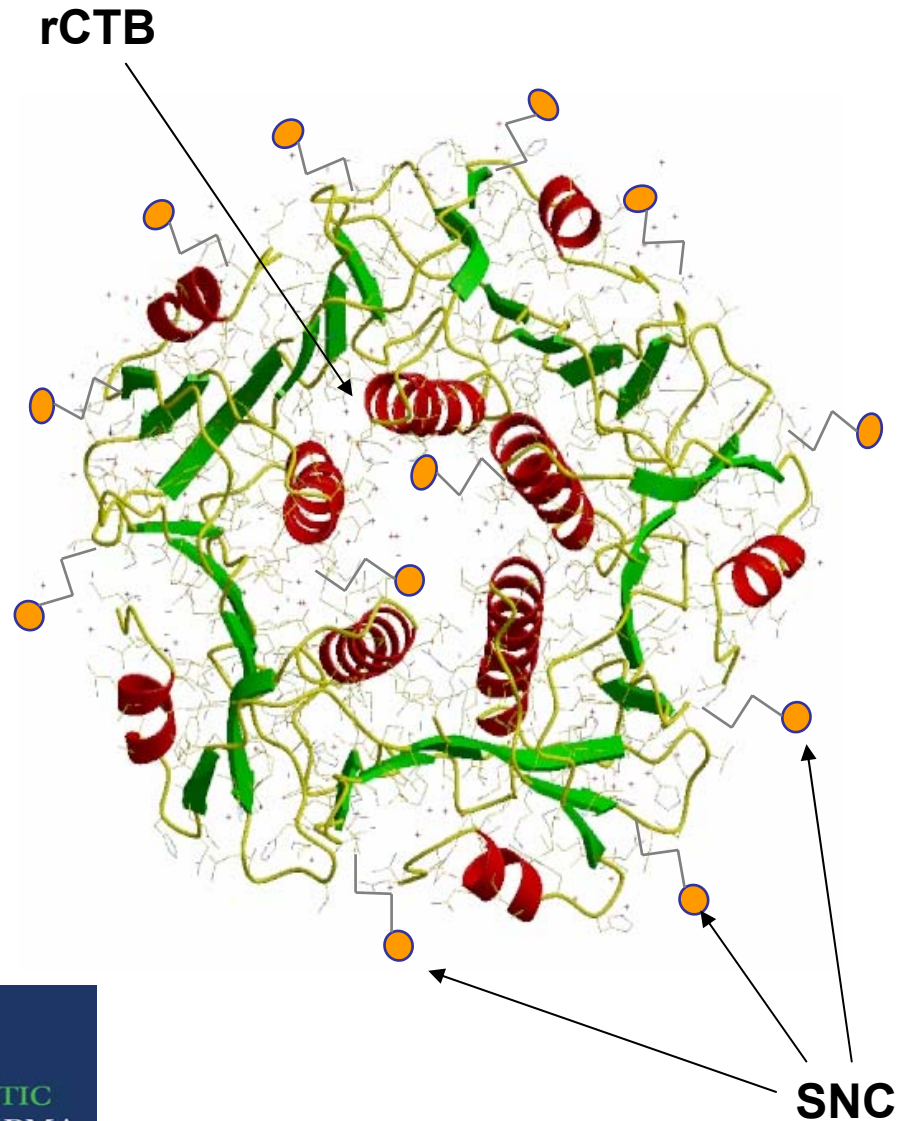
Blood:brain barrier

Brain



no "reward"

TA-CD Product Description

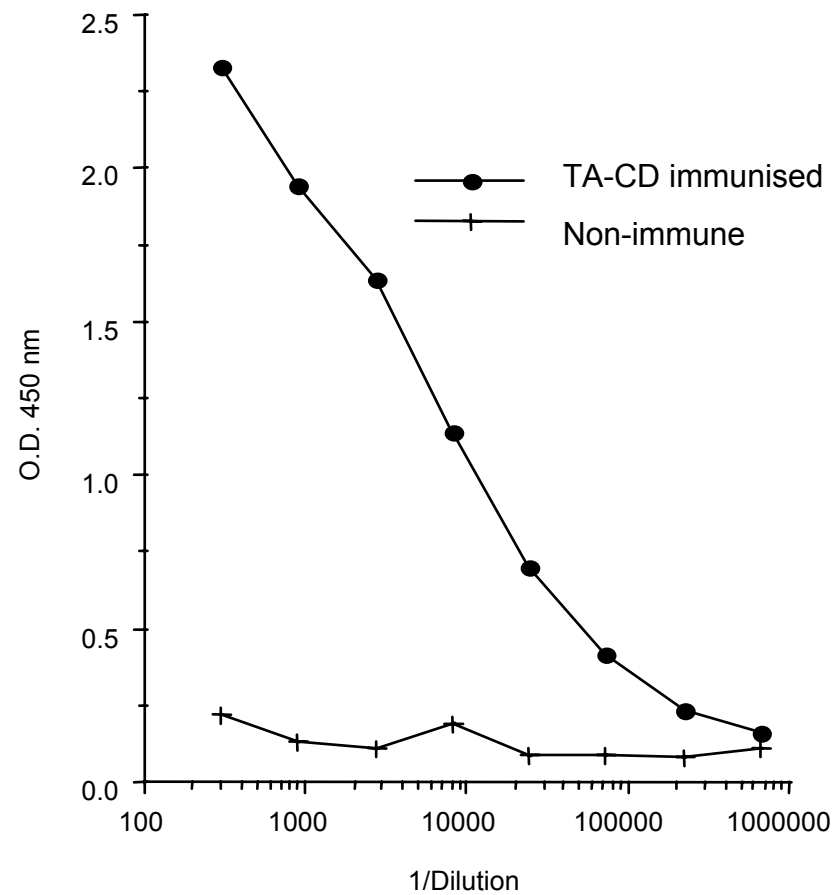


- **Cocaine derivative (succinyl norcocaine) coupled to recombinant cholera toxin B (rCTB)**
- **Linked by a stable covalent bond**
- **Aluminum hydroxide adjuvant added**
- **Given by intramuscular injection to upper arm**

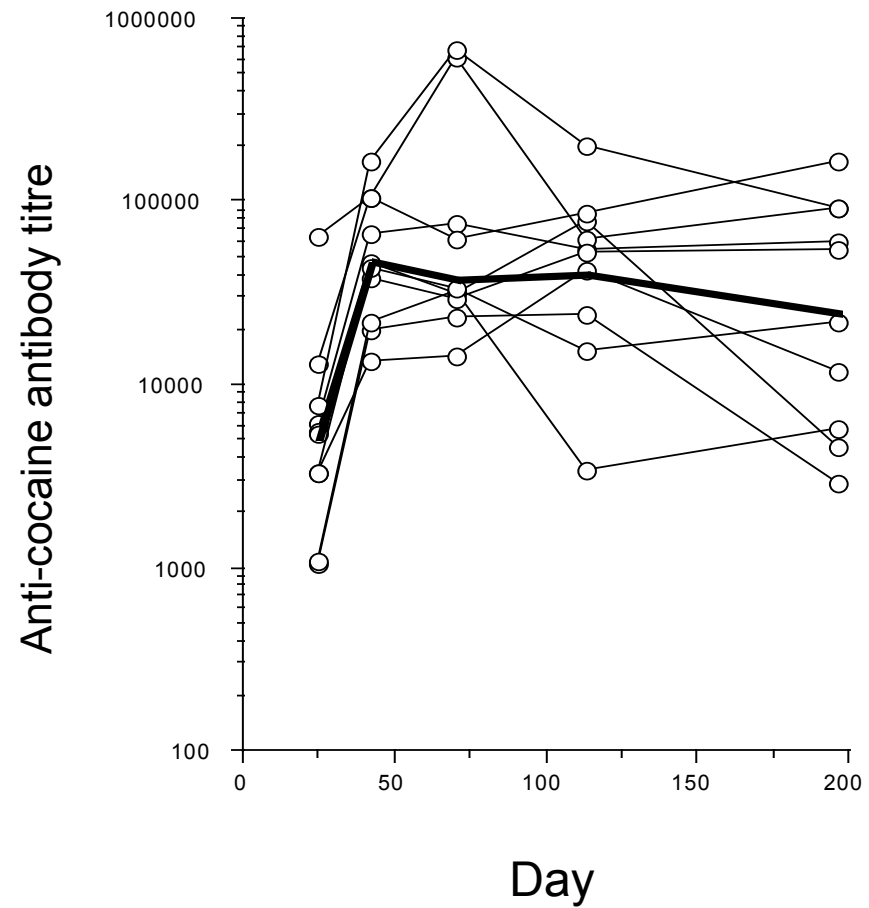
TA-CD – Preclinical Studies

- **Proof of concept established in pre-clinical models**
 - **Vaccine induces cocaine specific antibodies**
 - **Antibodies reduce levels of cocaine in brain**
 - **Vaccination leads to a significant reduction in cocaine self administration in addicted rodents**

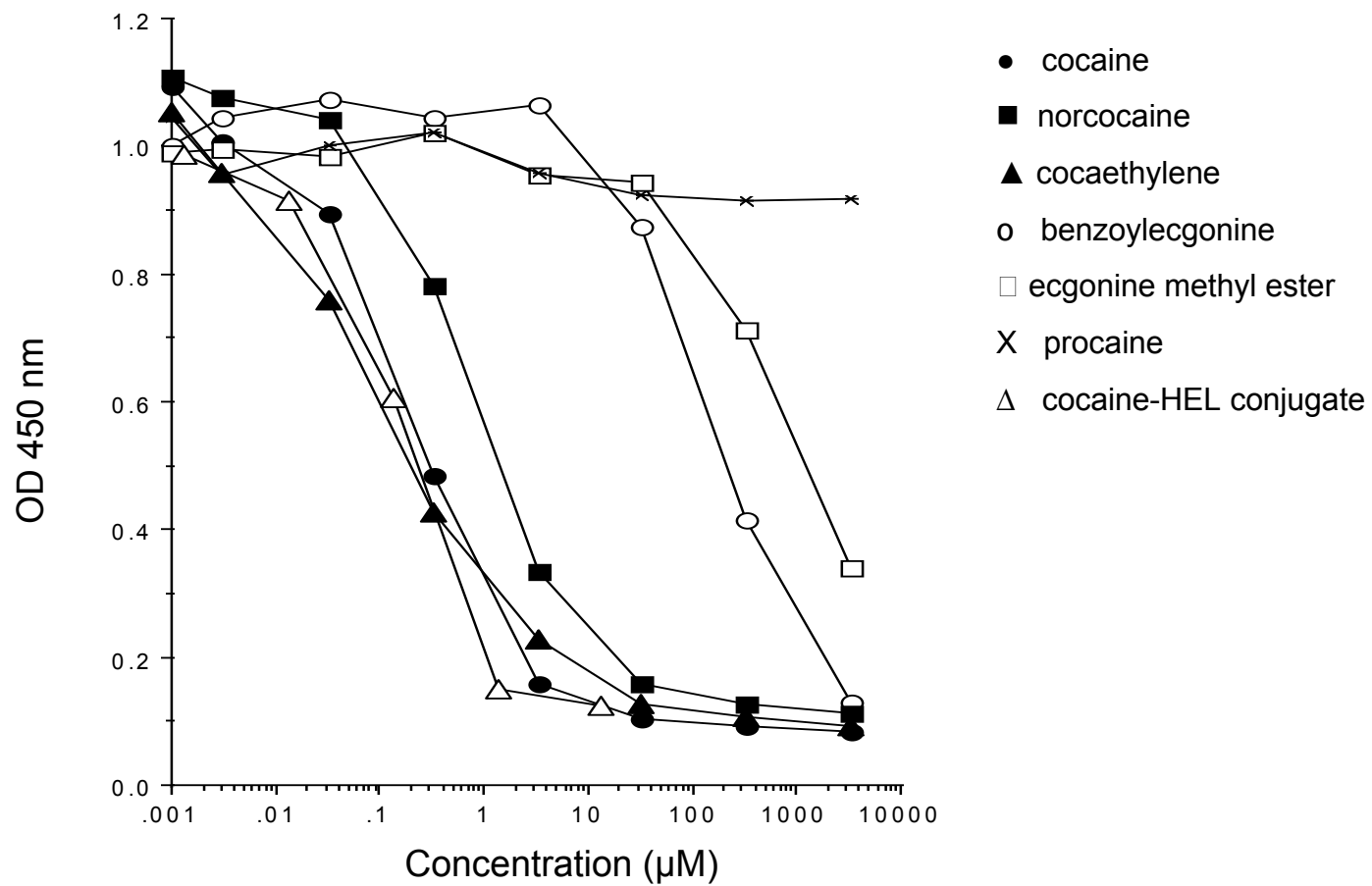
Immunogenicity of TA-CD in mice



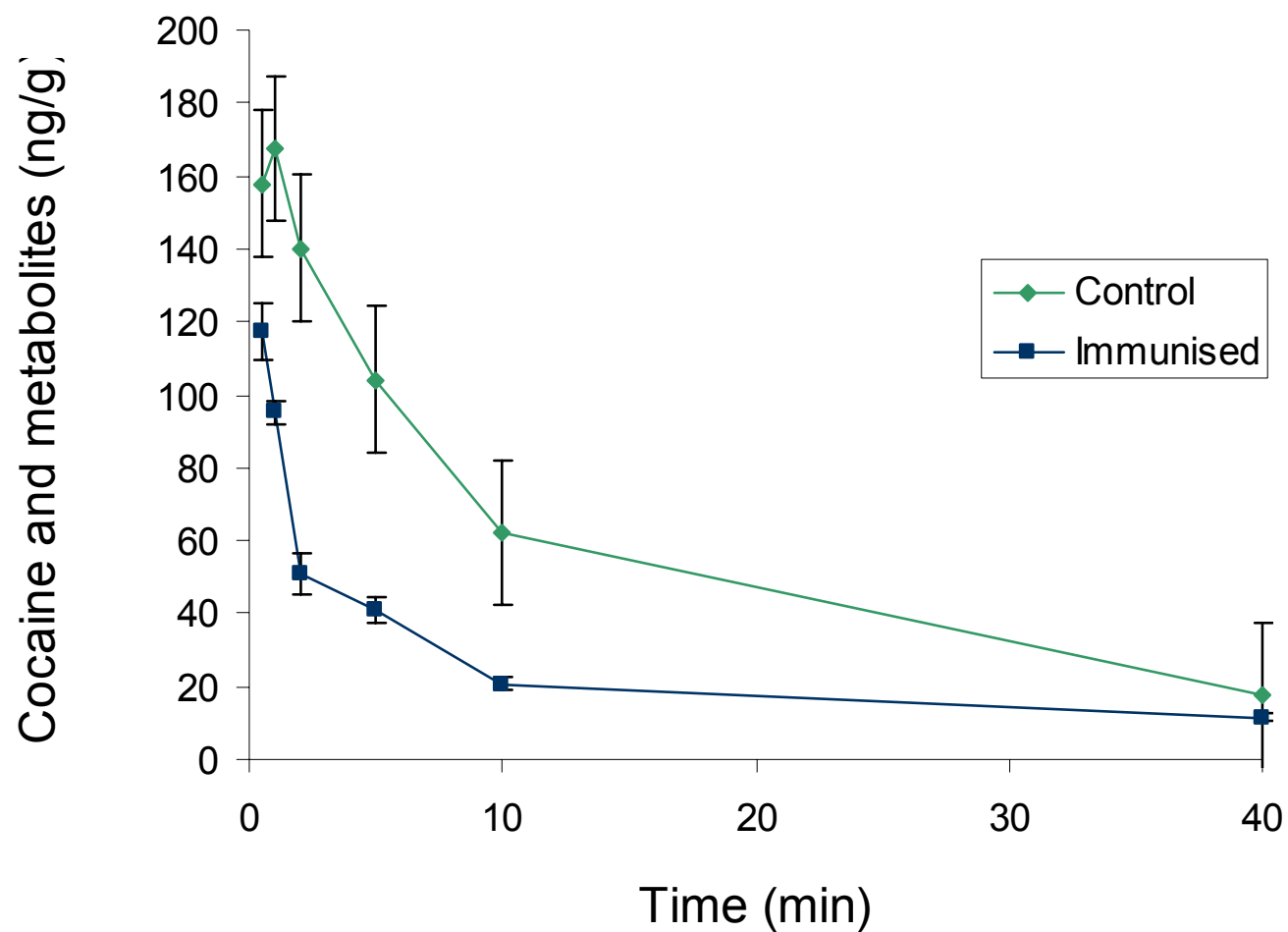
Duration of antibody response in mice



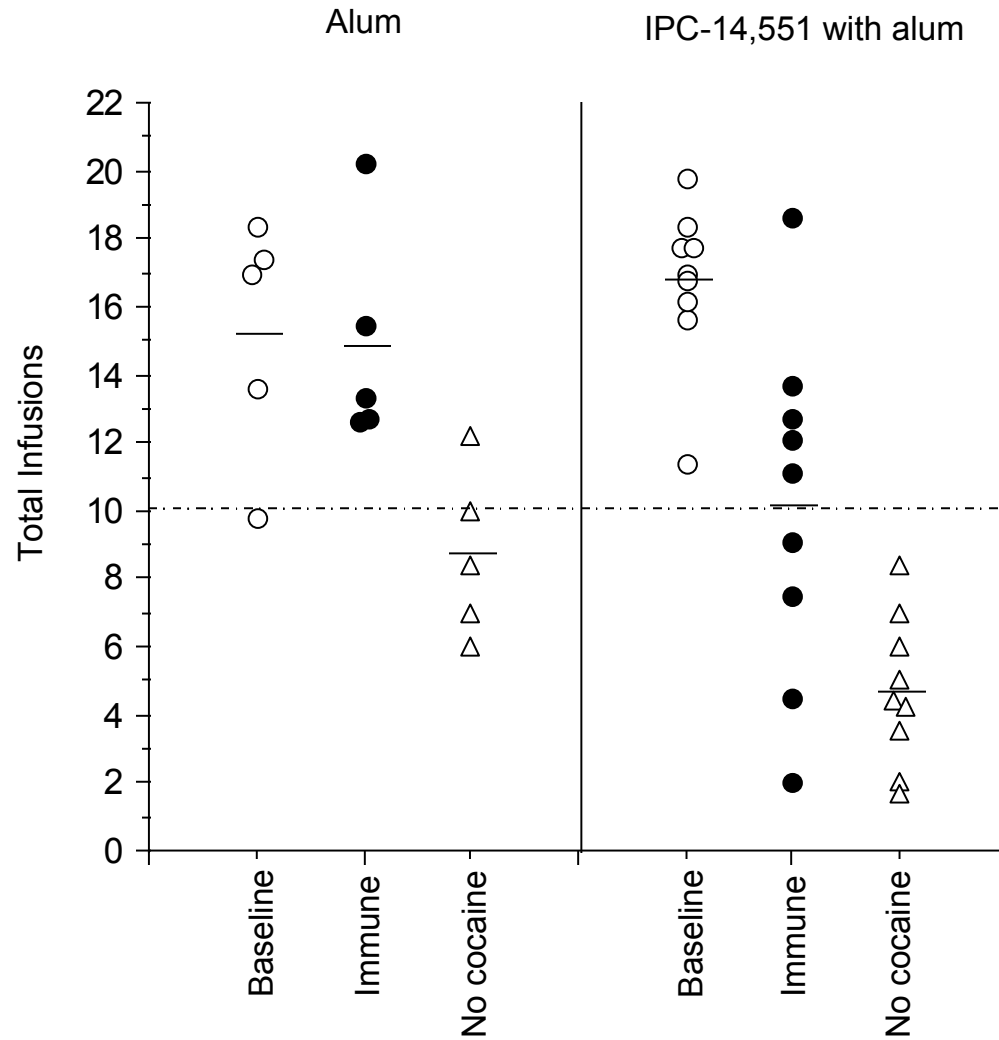
Specificity of immune response



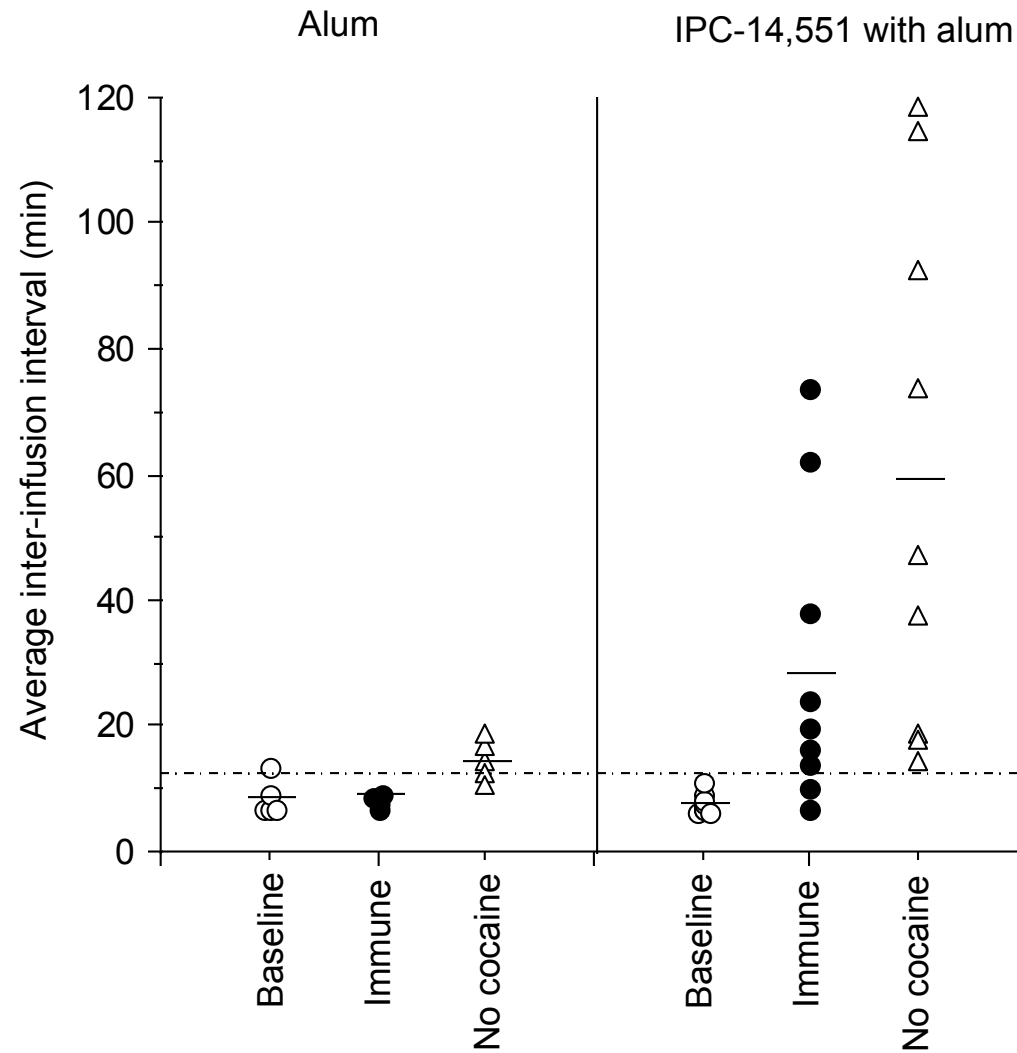
Loss of cocaine from brain in immunised mice



Effect of TA-CD on cocaine self-administration in rats (i)



Effect of TA-CD on cocaine self-administration in rats (ii)



TA-CD: Clinical Studies Summary

- **Completed:**
 - **Phase I: TA-CD/01 - Safety and Immunogenicity (n = 30)**
 - **Phase IIa: TA-CD/03 - Relapse Prevention (n = 9)**
 - **Phase IIa: TA-CD/06 - Abstinence Initiation (n = 13)**
- **In progress:**
 - **Phase IIa: TA-CD/04 – Cocaine Challenge (n=11)**
 - **Phase IIb: TA-CD/08 – Efficacy (randomised, double-blind placebo-controlled, n=132)**

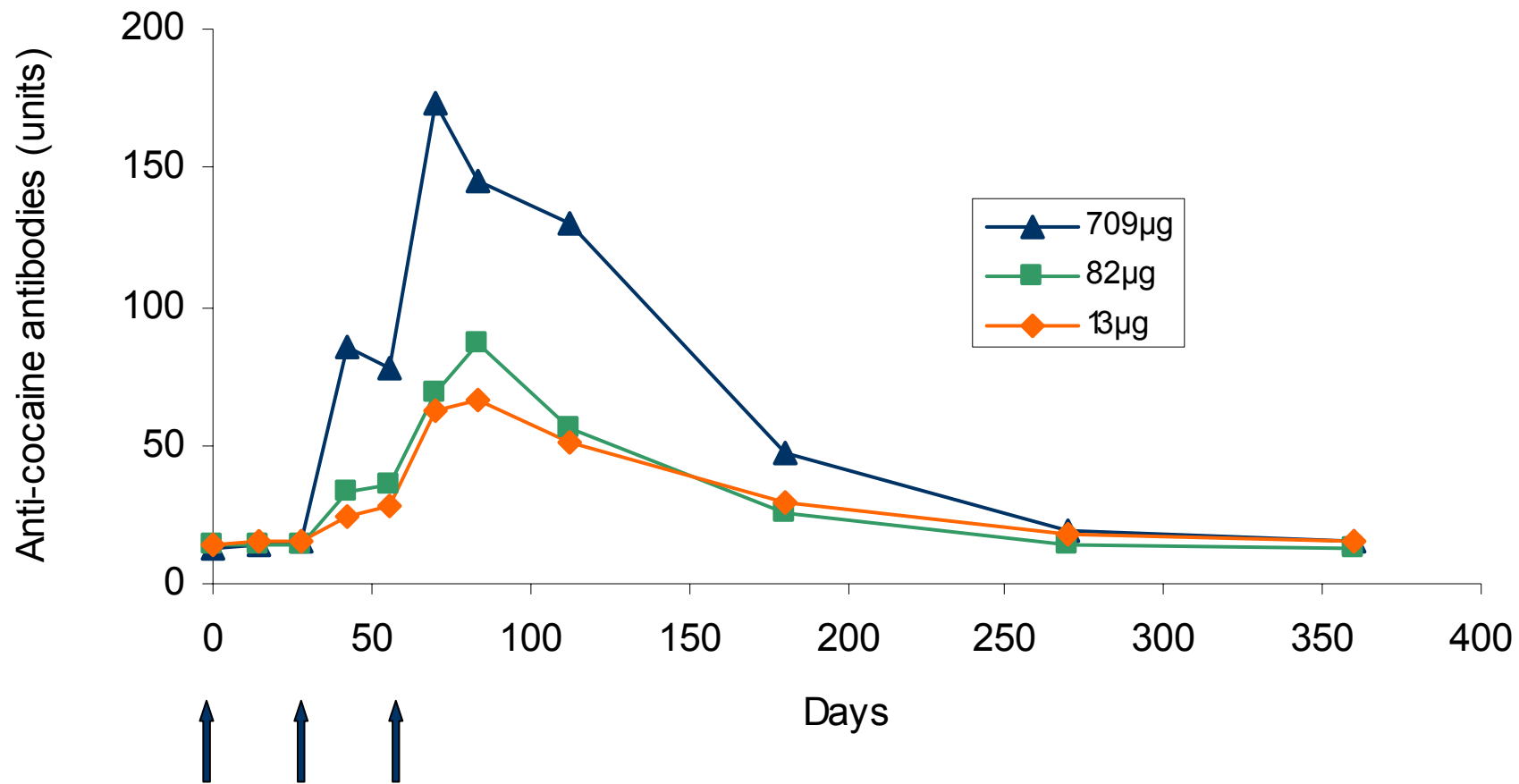
Phase I study design

- **Placebo-controlled double blind study**
- **30 cocaine abstinent subjects in in-patient facility**
- **Endpoints**
 - **Safety**
 - **Immunogenicity**
- **3 dose levels**
 - **13 µg, 82 µg, 709 µg**
- **Newtown Ct, USA, Prof Tom Kosten**

TA-CD Phase I study - safety

- **Vaccine well tolerated**
 - **Mild injection site reactions, also found in placebo group**
 - **No vaccine-related serious adverse events**
- **No significant difference in adverse events between placebo and active groups**

TA-CD – Phase I immunogenicity



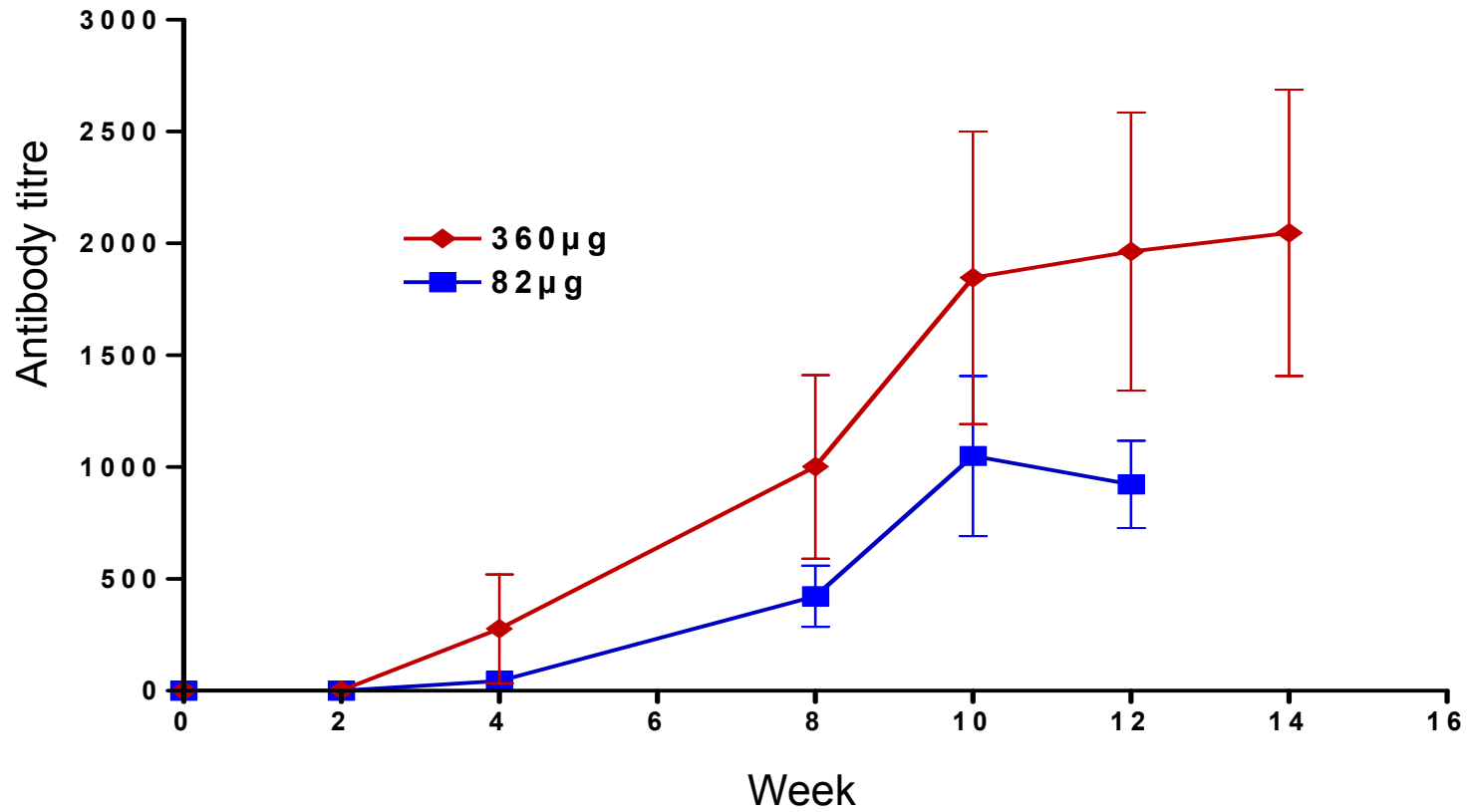
TA-CD Phase IIa Study Design

- **Two studies**
 - **Relapse Prevention (8 evaluable patients)**
 - **Abstinence Initiation (12 evaluable patients)**
- **Endpoints**
 - **Safety**
 - **Immunogenicity**
- **Two dose levels**
 - **82 µg, 360 µg**

TA-CD Phase IIa

- **Safety**
 - **Vaccine well tolerated**
 - **No vaccine-related serious adverse events**
 - **Some patients experienced mild injection site reactions**
- **Immunogenicity**
 - **Patients produced anti-cocaine antibodies in response to the vaccine**
 - **Higher dose generally resulted in higher antibody levels**
 - **Booster injection increased antibody levels which had dropped**

Phase IIa – Immunogenicity



TA-CD - Phase IIa - efficacy

- **Relapse prevention:**
 - **6/8 maintained abstinence during 12 wk study**
- **Abstinence initiation:**
 - **7/12 achieved & maintained abstinence during 12 wk study**
 - **5/12 remained cocaine free after 6 months**
- **Indication that higher antibody response correlates with reduced likelihood of using cocaine**
- **Some of those patients who relapsed post vaccination reported a reduction in euphoric effects of cocaine**

TA-CD - Phase IIb

- **Study design**
 - **132 methadone dependent cocaine addicts**
 - **Placebo controlled, randomized, double blind study**
- **Primary end point**
 - **Quit rate as determined by at least 3 consecutive weeks of negative urine samples between weeks 8-20**
- **Supported by NIDA**
- **Results due June 2006**

TA-CD – Future plans

- **If Phase II data are positive...**
- **Plan to move rapidly into**
 - **Phase III US**
 - **Phase III EU**
- **Challenges**
 - **Treatment of cocaine addicts varies from country to country**
 - medically
 - healthcare system
 - **Success depends on patient receiving full course of vaccinations**

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- **Phase IIb study (132 patients, randomised, placebo-controlled) is due to report June 2006**
- **Positive data will trigger a rapid move into Phase III studies**