

# **EUROPEAN URAEMIC TOXIN WORK GROUP**

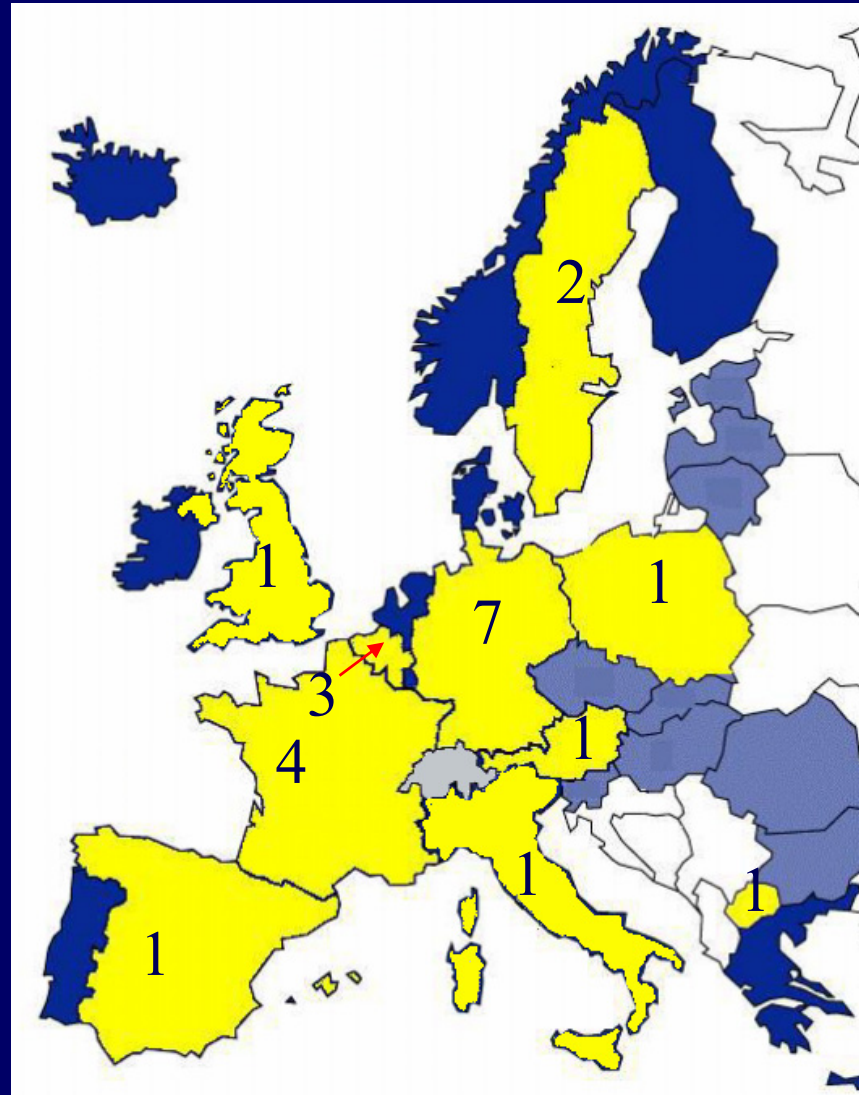


**SUMMARY OF ACTIVITIES  
(2000-2008)**

# EUROPEAN UREMIC TOXIN WORK GROUP (EUTox)

- ◆ A Argiles (F)
- ◆ U Baurmeister (G)
- ◆ J Beige (G)
- ◆ P Brouckaert (B)
- ◆ P Brunet (F)
- ◆ G Cohen (A)
- ◆ PP De Deyn (B)
- ◆ T Drüeke (F)
- ◆ D Fliser (G)
- ◆ S Herget-Rosenthal (G)
- ◆ W Hörl (A)
- ◆ J Jankowski (G)
- ◆ A Jörres (G)
- ◆ ZA Massy (F)
- ◆ H Mischak (G)
- ◆ A Perna (I)
- ◆ M Rodriguez (Sp)
- ◆ G Spasovski (Mac)
- ◆ B Stegmayr (Sw)
- ◆ P Stenvinkel (Sw)
- ◆ P Thornalley (UK)
- ◆ R Vanholder (B)
- ◆ C Wanner (G)
- ◆ A Wiecek (P)
- ◆ W Zidek (G)
- ◆ Amgen
- ◆ Bayer HealthCare
- ◆ Baxter Healthcare
- ◆ F. Hoffman – La Roche
- ◆ Fresenius Medical Care
- ◆ Gambro
- ◆ Genzyme
- ◆ Membrana
- ◆ Nipro
- ◆ Shire

# MEMBERS OF THE EUTox GROUP



# ACADEMIC INSTITUTES

## 1. Production and preparation of the molecules

Argiles (France); Brunet (France);  
Cohen/Hörl (Austria); Drüeke (France);  
Jörres (Germany); Jankowski (Germany);  
Massy (France); Rodriguez (Spain);  
Thornalley (UK); Vanholder (Belgium)

# ACADEMIC INSTITUTES

## 2. Study patho-physiologic mechanisms and elements

Argiles (France); Brunet (France); De Deyn (Belgium); Drüeke (France); Fliser (Germany); Herget-Rosenthal (Germany); Hörl (Austria); Jankowski (Germany); Jörres (Germany); Massy (France); Perna (Italy); Rodriguez (Spain); Stenvinkel (Sweden); Thornalley (UK); Vanholder (Belgium); Wiecek (Poland)

# ACADEMIC INSTITUTES

## 3. Clinical evaluation

**Argiles (France); Brunet (France); Drüeke (France); Fliser (Germany); Herget-Rosenthal (Germany); Hörl (Austria); Jörres (Germany); Massy (France); Perna (Italy); Rodriguez (Spain); Spasovski (Macedonia); Stegmayr (Sweden); Stenvinkel (Sweden); Vanholder (Belgium); Wanner (Germany); Wiecek (Poland)**

# ACADEMIC INSTITUTES

## 4. Genomics/proteomics

Argiles (France); Brouckaert (Belgium);  
Fliser (Germany); Janowski (Germany);  
Massy (France); Mischak (Germany); Perna  
(Italy); Rodriguez (Spain); Stenvinkel  
(Sweden); Wiecek (Poland)

# MEETINGS EUTox GROUP

## ◆ 2000

- Lausanne, Switzerland

## ◆ 2001

- Paris, France
- Cologne, Germany
- Gent, Belgium

## ◆ 2002

- Montpellier, France
- Vicenza, Italy
- Würzburg, Germany
- – Gent, Belgium

## ◆ 2003

- Cordoba, Spain
- Vienna, Austria
- Aachen, Germany
- Niedernberg, Germany

# MEETINGS EUTox GROUP

## ◆ 2004

- Marseille, France
- Berlin, Germany
- Vienna, Austria

## ◆ 2005

- Skopje, Macedonia
- Potsdam, Germany
- Brussels, Belgium

## ◆ 2006

- Potsdam, Germany
- Marseille, France
- Naples, Italy

## ■ ◆ 2007

- Krakow, Poland
- Essen, Germany
- Dresden/Leipzig, Germany

## ◆ 2008

- Sevilla, Spain

# MEETINGS EUTox GROUP

- **Symposium: “Uremic toxins and cardiovascular disease”**
- **October 3-5, 2008**
- **Amiens France** ■
- **Organization:**
  - » **Z Massy, President**
  - » **R Vanholder, Chairman EUTox**

# REVIEW/STATEMENT PUBLICATIONS I

**Vanholder et al.**

**Uremic toxicity: present state of the art**

***Int J Artif Org, 24, 695-725, 2001***

**Vanholder et al.**



**Uraemic toxins and cardiovascular disease**

***Nephrol Dial Transplant, 18, 463-466, 2003***

**Vanholder et al.**

**New insights in uremic toxins**

***Kidney Int, 63 (Suppl 84), S6-S10, 2003***

# UREMIC TOXINS WITH VASCULAR IMPACT

## Polymorphnuclear Neutrophils

Advanced glycation products  
 Advanced oxidation protein products  
 Angiogenin (DIP I)  
 Complement factor D (DIP II)  
 Cytokines  
 Ig Light chains  
 Leptin

## Endothelial Cells

Advanced glycation products  
 Advanced oxidation protein products  
 $\beta$ 2-microglobulin  
 Cytokines  
 Homocysteine  
 Leptin  
 Oxalic Acid  
 Oxidized LDL

## Platelets

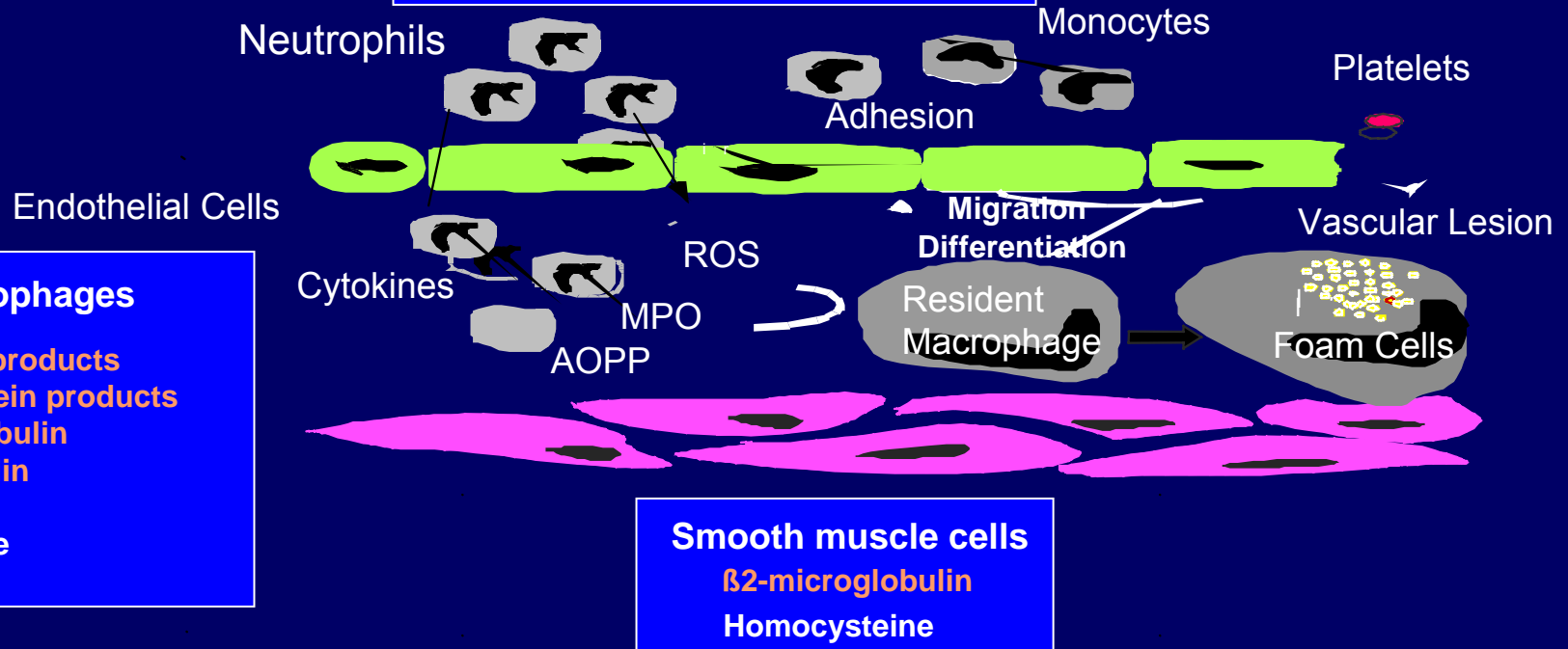
Cytokines  
 Leptin

## Monophages/Macrophages

Advanced glycation products  
 Advanced oxidation protein products  
 AGE- $\beta$ 2-microglobulin  
 $\beta$ 2-microglobulin  
 Cytokines  
 Homocysteine  
 Leptin

## Smooth muscle cells

$\beta$ 2-microglobulin  
 Homocysteine



# REVIEW/STATEMENT PUBLICATIONS I

**Vanholder et al.**

**Uremic toxicity: present state of the art**

***Int J Artif Org, 24, 695-725, 2001***



**Vanholder et al.**

**Uraemic toxins and cardiovascular disease**

***Nephrol Dial Transplant, 18, 463-466, 2003***

**Vanholder et al.**

**New insights in uremic toxins**

***Kidney Int, 63 (Suppl 84), S6-S10, 2003***

# REVIEW/STATEMENT PUBLICATIONS II

**Vanholder et al.**

**Review on uremic toxins: classification, concentration and interindividual variability**

***Kidney Int, 63, 1934-1943, 2003***



**Vanholder et al.**

**Chronic kidney disease as cause of cardiovascular morbidity and mortality**

***NDT, 20, 1048-1056, 2005***

**Vanholder et al.**

**The European artificial organ scene**

***Artif Organs, 29, 498-506, 2005***

# UREMIC SOLUTES LISTED

**Small water soluble compounds (<500D):** 1-Methyladenosine, 1-Methylguanosine, 1-Methylinosine, ADMA,  $\gamma$ -Keto-guanidinovaleric acid,  $\alpha$ -N-acetylarginine, Arab(in)itol, Argininic acid, Benzylalcohol,  $\beta$ -guanidinopropionic acid, Creatine, Creatinine, Cytidine, Dimethylglycine, Erythritol,  $\gamma$ -guanidinobutyric acid, Guanidine, Guanidinoacetic acid, Guanidonosuccinic acid, Hypoxanthine, Mannitol, Methylguanidine, Myoinositol, N4-acetylcytidine, N6-methyladenosine, Orotic acid, Orotidine, Oxalate, Phenylacetylglutamine, Pseudouridine, SDMA, Sorbitol, Taurocyamine, Threitol, Thymine, Uracil, Urea, Uric acid, Uridine, Xanthine, Xanthosine

**Protein-bound molecules:** 2-Methoxyresorcinol, 3-deoxyglucosone, CMPF, Dimethylguanosine, Fructoselysine, Glyoxal, Hippuric acid, Homocysteine, Hydroquinone, Indole-3-acetic acid, Indoxyl sulfate, Interleukin 1 $\beta$ , Interleukin 6, Kinurenine, Kynurenic acid, Leptin, Melatonin, Methylglyoxal, N-(carboxymethyl)lysine, P-cresol, Pentosidine, Phenol, Phenylacetic acid, Phenylethylamine, P-OHhippuric acid, Putrescine, Quinolinic acid, Retinol binding protein, S-nitrosothiol, Spermidine, Spermine, Thiocyanate, Tumor Necrosis Factor  $\alpha$

**Middle molecules (>500D):** Adrenomedullin, Atrial natriuretic peptide,  $\beta$ 2-microglobulin,  $\beta$ -endorphin, Cholecystikinin, Clara cell protein, Complement factor D, Cystatin C, Degranulation inhibiting protein I, Delta-sleep inducing peptide, Endothelin (ng/L), Ghrelin, Hyaluronic acid, Interleukin 1 $\beta$ , Interleukin 6, Interleukin-18,  $\kappa$ -Ig light chain,  $\lambda$ -Ig light chain, Leptin, MC-SF, Methionine-enkephalin, Neuropeptide Y, Orexin A, Parathyroid hormone, Retinol binding protein, Tumor Necrosis Factor  $\alpha$



# REVIEW/STATEMENT PUBLICATIONS III

**Vanholder et al.**

**Chronic kidney disease as cause of cardiovascular morbidity and mortality**

***NDT, 20, 1048-1056, 2005***

**Vanholder et al.**



**The European artificial organ scene**

***Artif Organs, 29, 498-506, 2005***

**Meert et al.**

**Inconsistency of reported uremic toxin concentrations**

***Artif Organs, 31, 600-611, 2007***

# REVIEW/STATEMENT PUBLICATIONS IV

**Vanholder et al.**

**Review on uremic solutes II – Variability in reported concentrations: causes and consequences**  
*NDT, 2007, in press*

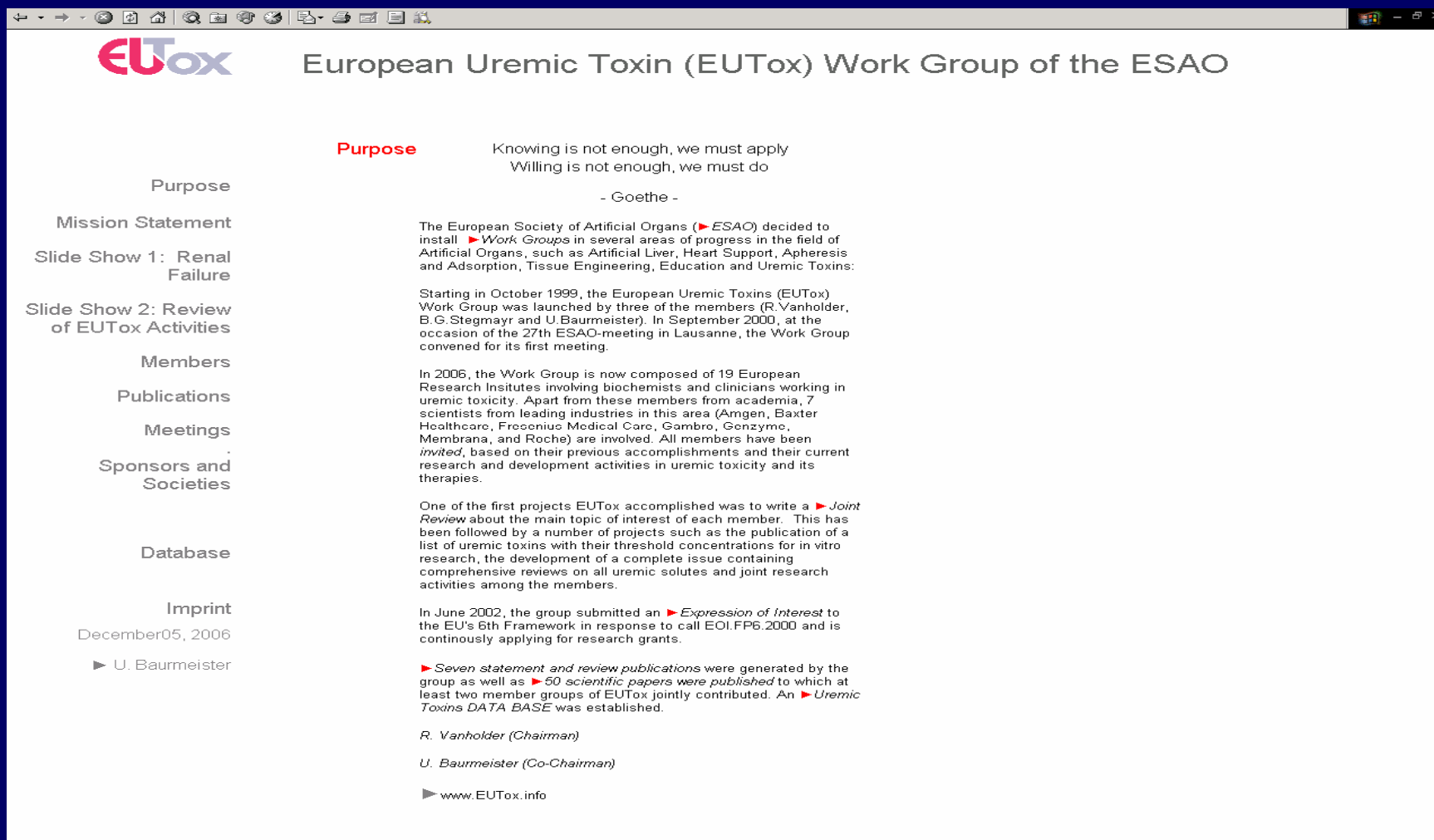


**Cohen et al.**

**Review on uremic solutes III – Recommendations for handling uraemic retention solutes in vitro: towards a standardised approach for research on uraemia**  
*NDT, 2007, in press*

# WEBSITE OF THE EUTox GROUP

## www.uremic-toxins.org



The screenshot shows a web browser window displaying the website for the European Uremic Toxin (EUTox) Work Group of the ESAO. The browser's address bar is empty, and the page title is "European Uremic Toxin (EUTox) Work Group of the ESAO". The website features a navigation menu on the left side with the following items: Purpose, Mission Statement, Slide Show 1: Renal Failure, Slide Show 2: Review of EUTox Activities, Members, Publications, Meetings, Sponsors and Societies, Database, Imprint, and December05, 2006. The main content area is titled "Purpose" and contains the following text:

**Purpose** Knowing is not enough, we must apply  
Willing is not enough, we must do  
- Goethe -

The European Society of Artificial Organs (► **ESAO**) decided to install ► **Work Groups** in several areas of progress in the field of Artificial Organs, such as Artificial Liver, Heart Support, Apheresis and Adsorption, Tissue Engineering, Education and Uremic Toxins:

Starting in October 1999, the European Uremic Toxins (EUTox) Work Group was launched by three of the members (R. Vanholder, B.G. Stegmayr and U. Baurmeister). In September 2000, at the occasion of the 27th ESAO-meeting in Lausanne, the Work Group convened for its first meeting.

In 2005, the Work Group is now composed of 19 European Research Institutes involving biochemists and clinicians working in uremic toxicity. Apart from these members from academia, 7 scientists from leading industries in this area (Amgen, Baxter Healthcare, Fresenius Medical Care, Gambro, Genzyme, Membrana, and Roche) are involved. All members have been *invited*, based on their previous accomplishments and their current research and development activities in uremic toxicity and its therapies.

One of the first projects EUTox accomplished was to write a ► **Joint Review** about the main topic of interest of each member. This has been followed by a number of projects such as the publication of a list of uremic toxins with their threshold concentrations for in vitro research, the development of a complete issue containing comprehensive reviews on all uremic solutes and joint research activities among the members.

In June 2002, the group submitted an ► **Expression of Interest** to the EU's 6th Framework in response to call EOI.FP6.2000 and is continuously applying for research grants.

► **Seven statement and review publications** were generated by the group as well as ► **50 scientific papers** were published to which at least two member groups of EUTox jointly contributed. An ► **Uremic Toxins DATA BASE** was established.

*R. Vanholder (Chairman)*  
*U. Baurmeister (Co-Chairman)*

► [www.EUTox.info](http://www.EUTox.info)

# UREMIC TOXINS DATABASE OF EUTox GROUP

www.EUTox.info

EUTox Uremic Toxin Database

[About](#) - [View Toxins](#) - [Log in](#) - [Become a member](#)

**View toxins in database**

Choose one or more toxins from the list below. Use CTRL to select multiple toxins.

Available Toxins:	Show:
1-Methyladenosine	<input checked="" type="checkbox"/> Master of Molecule <input type="checkbox"/> CU/CN
1-Methylguanosine	<input checked="" type="checkbox"/> Normal Concentration (CN) <input type="checkbox"/> CM/CN
1-Methylinosine	<input checked="" type="checkbox"/> Standard Deviation of CN <input type="checkbox"/> CM/CU
2-Methoxyresorcinol	<input checked="" type="checkbox"/> Sample Number of CN <input type="checkbox"/> Molecular Weight
3-Deoxyglucosone	<input checked="" type="checkbox"/> Uremic Concentration (CU) <input type="checkbox"/> Substance Type
ADMA	<input checked="" type="checkbox"/> Standard Deviation of CU <input type="checkbox"/> References
Adrenomedullin	<input checked="" type="checkbox"/> Sample Number of CU
Alpha-keto-Delta-Guanidinovaleic Acid	<input checked="" type="checkbox"/> Maximum Concentration (CM)
Alpha-N-Acetylarginine	
Arab(in)itol	
Argininic Acid	
Atrial Natriuretic Peptide	
Benzylalcohol	
Beta-2-Microglobulin	
Beta-Endorphin	
Beta-Guanidinopropionic Acid	

Sort by:  
Name  
 Ascending (0-9, A-Z)  
 Descending (Z-A, 9-0)

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# 59 JOINT PUBLICATIONS

## ◆ 2002

- Clin Chem
- Circulation

## ◆ 2004

- JASN (2)

## ◆ 2005

- JASN (3)
- Nat Med
- Hypertension
- Circulation

## ◆ 2006

- Proteomics

## ◆ 2007

- – JASN
- Proteomics
- Arterioscler  
Thromb Vasc Biol

## ◆ 2008

- JASN

# **CURRENT RESEARCH ACTIVITIES OF THE EUTOX GROUP**

**Investigation of effects of uremic toxins on:**

- **Endothelial cell function**
- **Thrombocyte aggregation**
- **NADPH oxidase activity, leukocyte free radical production**
- **Vascular smooth muscle cell reactivity**
- **Tubular cells**
- **Fibroblasts**

# AIMS FUTURE RESEARCH

## 1. *In vitro* studies

Identification of uremic toxins responsible for vascular damage (effect on the 4 major cell systems involved: endothelium, leukocytes, thrombocytes, smooth muscle cells)

## 2. *In vivo* studies

Identification of mechanisms leading to vascular damage in CKD

# AIMS FUTURE RESEARCH MORE EMPHASIS ON:

1. *Proteomics*
2. *Genomics* ■
3. *Metabolomics*