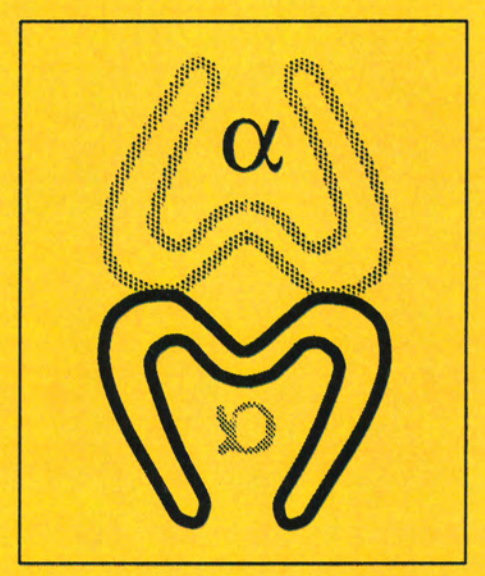
THIRD INTERNATIONAL WORKSHOP ON

α_2 - MACROGLOBULIN AND RELATED PLASMA PROTEINS : STRUCTURE , FUNCTION , REGULATION

OCTOBER 24 - 27 , 1990



P R O G R A M

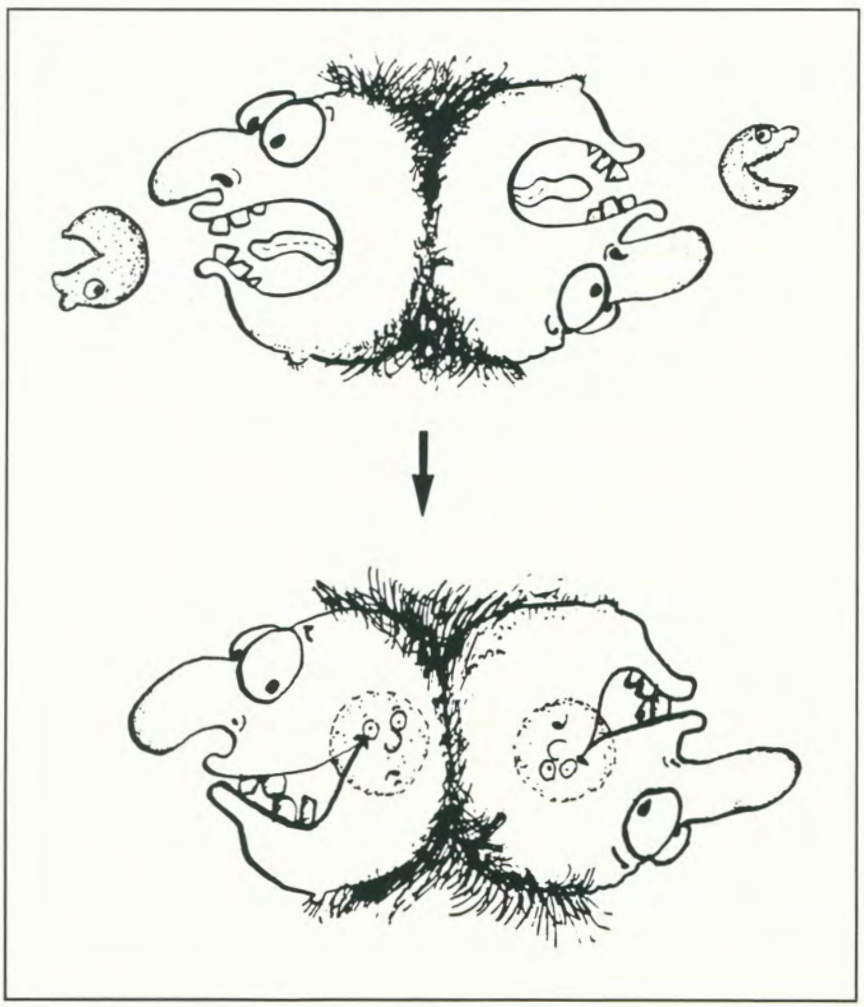
START OF THE WORKSHOP

Wednesday OCTOBER 24, 1990

Arrivals

7.00-10.00 p.m. **Mixer - Drinks and Snacks**

(Zahn 7, Neuklinikum, level E, elevator C6, corridor 48)



alpha2-macroglobulin, a proteinase-trap

Thursday morning — OCTOBER 25, 1990

8.25- 8.30 a.m.	Introduction	**P.C. Heinrich** (Aachen, FRG)

(1) Structural Studies on α-Macroglobulins

Moderators: **R. Feinman** (New York, USA)
P. Gettins (Nashville, USA)

		Speakers
8.30- 8.50 a.m.	Localization of small ligands in transformed α_2-macroglobulin (electron microscopy and image processing)	**E. Delain** (Villejuif, France)
8.50- 9.10 a.m.	Localization of specific site-linked protein to α_2-macroglobulin by image processing	**F. Pochon** (Orsay, France)
9.10- 9.30 a.m.	Immunochemical studies of α_2-macroglobulin and pregnancy zone protein	**P.E. Jensen, T. Stigbrand** (Umea, Sweden)
9.30- 9.50 a.m.	Surface properties of α-macroglobulins analyzed by affinity phase partitioning	**G. Birkenmeier** (Leipzig, DDR)

9.50-10.20 a.m. **Coffee break**

Thursday morning — OCTOBER 25, 1990

		Speakers
10.20-10.40 a.m.	Measurement of the separation between thiol groups in fast form α_2-macroglobulin using fluorescence energy transfer	**P. Gettins** (Nashville, USA)
10.40-11.00 a.m.	Solution structures of monomeric, dimeric and tetrameric thiolester-proteins	**R. Österberg** (Uppsala, Sweden)
11.00-11.20 a.m.	The specific recognition of conformational changes in α_2-macroglobulin by bacterial surface proteins	**H.-P. Müller** (Uppsala, Sweden)
11.20-11.40 a.m.	Kinetics of the conformational change of α_2-macroglobulin observed with X-ray solution scattering and fluorescence	**H. Arakawa** (Nagatsuta, Japan)
11.40-12.00 a.m.	Expression of wild type human α_2-macroglobulin and a bait region mutant in hamster kidney fibroblasts	**E. Boel** (Bagsvaerd, Denmark)

12.00- 3.00 p.m. **Lunch break**

Thursday afternoon **OCTOBER 25, 1990**

(2) Regulation of α-Macroglobulin Biosynthesis

Moderators: **J. Gliemann** (Aarhus, Denmark)
L. Sevaljevic (Belgrade, Yugoslavia)

		Speakers
3.00-3.25 p.m.	Murine α_2-macroglobulin	**F. Van Leuven** (Leuven, Belgium)
3.25-3.40 p.m.	Molecular cloning and sequencing of murinoglobulin cDNAs	**L.Overbergh** (Leuven, Belgium)
3.40-4.00 p.m.	Gene structure of human α-macroglobulins	**P. Marynen** (Leuven, Belgium)
4.00-4.20 p.m.	Hormonal regulation of pregnancy-associated murine protein-1	**J. Hau** (Copenhagen, Denmark)

4.20-4.50 p.m. **Coffee break**

Thursday afternoon — OCTOBER 25, 1990

		Speakers
4.50-5.10 p.m.	Synthesis and role of α_2-macroglobulin in scalded rats	**L. Sevaljevic** (Belgrade, Yugoslavia)
5.10-5.30 p.m.	Role of interleukin-6 and its hepatic receptor in rat α_2-macroglobulin gene expression	**F. Horn** (Aachen, FRG)
5.30-5.50 p.m.	Properties of nuclear proteins from rat liver that bind at the IL-6-response element of the α_2-macroglobulin gene	**T. Brechner** (La Jolla, USA)
5.50-6.10 p.m.	Changes in the glycosylation of α_2-macroglobulin under pathological conditions	**W. Boers** (Amsterdam, Netherlands)
6.10-6.30 p.m.	In situ analysis of the expression of three acute phase protein genes (α_2-macroglobulin, α_1-inhibitor 3 and α_1-antitrypsin) in normal liver and in stimulated liver during the acute inflammatory reaction in the rat	**G. Feldmann** (Paris, France)

Friday morning — OCTOBER 26, 1990

(3) α_2-Macroglobulins of Different Species

Moderator: S. Law (Oxford, UK)

		Speakers
8.30- 8.45 a.m.	α_2-Macroglobulin from *Limulus polyphemus*	**J. Quigley** (Stoney Brook, USA)
8.45- 9.00 a.m.	α_2-Macroglobulin in invertebrates	**P. Armstrong** (Davis, USA)
9.00- 9.15 a.m.	Searching for thioester-containing proteins in invertebrates (*Homarus americanus*)	**S. Spycher** (Bern, Switzerland)
9.15- 9.30 a.m.	Immunogenetics of α-macroglobulins from mink and pig	**V.I. Ermolaev** (Novosibirsk, USSR)
9.30- 9.45 a.m.	Mink serum α-macroglobulins: Purification and biochemical properties	**L.M. Skobeltsina** (Novosibirsk, USSR)

9.45-10.15 a.m. **Coffee break**

Friday morning — **OCTOBER 26, 1990**

(4) α_2-Macroglobulin as Scavenger

Moderator: **D. Strickland** (Rockville, USA)

		Speakers
10.15-10.40 a.m.	Enzymatically catalyzed and non-enzymatic binding of polypeptides to α_2-macroglobulin	**W. Borth** (New York, USA)
10.40-11.00 a.m.	Binding of non-proteolytic proteins to α_2-macroglobulin	**K. Keck** (Konstanz, FRG)
11.00-11.20 a.m.	α_2-Macroglobulin and pregnancy zone protein: Comparison on binding specifities for nerve growth factor and transforming growth factor-beta, and their roles in hormone catabolism	**P.H. Koo** (Rootstown, USA)
11.20-11.40 a.m.	α_2-Macroglobulin as a scavenger of TGBβ: Production by myofibroblast-like cells - a potential role as feedback regulator	**M.G. Bachem** (Marburg, FRG)
11.40-12.00 a.m.	Inhibition of TGF-β_1-α_2M complex formation by polyanionic polysaccharides	**T. McCaffrey** (New York, USA)
12.00-12.20 p.m.	Binding properties of the α-macroglobulin-related proteins, complement components C3 and C4	**S. Law** (Oxford, UK)

12.20- 3.00 p.m. **Lunch break**

Friday afternoon — OCTOBER 26, 1990

(5) Protease Trapping I

Moderators: **F. Van Leuven** (Leuven, Belgium)
L. Sottrup-Jensen (Aarhus, Denmark)

		Speakers
3.00-3.25 p.m.	Localization of ϵ-lysyl-γ-glutamyl cross-links in five human α_2-macroglobulin proteinase complexes. Nature of the high molecular weight cross-linked products	**L. Sottrup-Jensen** (Aarhus, Denmark)
3.25-3.45 p.m.	The bait region	**G. Salvesen** (Durham, USA)
3.45-4.05 p.m.	Intramolecular localization of proteases within α_2-macroglobulin by image processing	**N. Boisset** (Tours, France)
4.05-4.25 p.m.	The mechanism of pregnancy zone protein-protease interactions	**U. Christensen** (Copenhagen, Denmark)
4.25-4.45 p.m.	Identification of a high-molecular-mass cysteine proteinase as an α-macroglobulin cathepsin-complex	**B. Dahlmann** (Düsseldorf, FRG)

4.45-5.15 p.m. **Coffee break**

Friday afternoon — OCTOBER 26, 1990

		Speakers
5.15-5.40 p.m.	Covalent bond formation in α_2-macroglobulin	**R. Feinman** (New York, USA)
5.40-6.00 p.m.	Complex formation between α_2-macroglobulin and glandular kallikrein	**H. Koh** (Martinsried, FRG)
6.00-6.20 p.m.	Interaction of α_2-macroglobulin and medullasin (a serine protease in bone marrow cells)	**Y. Aoki** (Tokyo, Japan)
6.20-6.40 p.m.	Interaction of matrix metalloproteinases with α_2-macroglobulin	**H. Nagase** (Kansas City, USA)

8.00 p.m. **Workshop Dinner at the Restaurant "Ratskeller"**

Am Markt

Saturday morning — OCTOBER 27, 1990

(5) Protease Trapping II

Moderator: **T. Stigbrand** (Umea, Sweden)

		Speakers
8.30- 8.50 a.m.	Tumor-associated α_2-macroglobulin: Regulation of plasminogen activation and growth factor activity	**A. Vaheri** (Helsinki, Finland)
8.50- 9.10 a.m.	Potential biological significance of the affinity between plasmin and pregnancy-associated α_2-glycoprotein (α_2PAG, PZP)	**J. Hau** (Copenhagen, Denmark)
9.10- 9.30 a.m.	Human antileukoproteinase: Expression in E.coli and functional characterization of this potent inhibitor of human leukocyte elastase	**R. Heinzel-Wieland** (Aachen, FRG)

9.30-10.00 a.m. **Coffee break**

Saturday morning — **OCTOBER 27, 1990**

(6) α_2M-Receptor/Endocytosis

Moderator: **S. Pizzo** (Durham, USA)

		Speakers
10.00-10.25 a.m.	High affinity Ca^{2+} binding to α_2MR determines receptor conformation and ligand recognition	**J. Gliemann** (Aarhus, Denmark)
10.25-10.50 a.m.	Structural studies on the α_2-macroglobulin receptor	**D. Strickland** (Rockville, USA)
10.50-11.10 a.m.	Structural analysis of human placental α_2M-receptor	**T. Kristensen** (Aarhus, Denmark)
11.10-11.30 a.m.	The α_2-macroglobulin receptor in the regulation of growth factor activity	**S.L. Gonias** (Charlottesville, USA)
11.30-11.55 a.m.	α_2-macroglobulin receptor recognition and signal transduction	**S. Pizzo** (Durham, USA)

END OF THE WORKSHOP

Biol. Chem. Hoppe-Seyler
Vol. 372, pp. 129–148, March 1991

87. Konferenz der Gesellschaft für Biologische Chemie

α_2-Macroglobulin and Related Plasma Proteins

Structure, Function, Regulation

Held in Aachen, October 24–27, 1990
Organized by P.C. Heinrich

Sponsored by Deutsche Forschungsgemeinschaft (Bonn–Bad Godesberg), Falk Foundation e.V. (Freiburg/Br.), Gesellschaft für Biologische Chemie, Grünenthal GmbH (Stolberg), Hoechst AG (Frankfurt/M.), MSD Sharp & Dohme GmbH (München), Nattermann & Cie. GmbH (Köln), Paul-Martini-Stiftung (Bonn), Schering AG (Berlin)

Abstracts (in the alphabetical order of first authors)

Y. Aoki, T. Hase and A. Ikai

Interaction of α_2-Macroglobulin and Medullasin (a Serine Protease in Bone Marrow Cells)

Both α_2-macroglobulin (α_2-M) and ovomacroglobulin (OMG) inhibited medullasin activity at equimolar or less ratios. SDS-gel electrophoretic patterns of α_2-M and OMG incubated with medullasin showed cleavage at the bait region with no further degradation. When the protease was added to a mixture of α_2-M and α_1-antitrypsin(α_1-AT) (molar ratio; 1:2:30), the esterase activity of medullasin decreased to 63% of the control. When human serum was diluted to 1/10 or 1/30 and mixed with medullasin, its activity decreased to 35% of the original. In the whole serum, therefore, 30-40% of medullasin is considered to be inhibited by α_2-M, and 60-70% by α_1-AT and other inhibitors[1]. Medullasin is quite similar to elastase in that the amino acid sequence from N-terminal to Gln^{218} is identical with that of leukocyte elastase and medullasin hydrolyzes synthetic substrates for elastase and is inhibited by its inhibitors[2]. However, it is not an elastase because medullasin is devoid of elastinolytic activity. When elastin fibers prepared by four representative methods[3-6] and stained with orcein were employed as substrate, medullasin revealed only a negligible (below 0.3% of pancreas elastase) elastinolytic activity. Injection of medullasin into the animal skin caused inflammation characterized by the infiltration of macrophages. Injection of equimolar mixture of medullasin and α_2-M caused no inflammatory reactions. When α_2-M was injected 5 seconds after medullasin injection, inflammation occured to the same degree as when only medullasin was injected. Therefore, exposure of tissues to medullasin for a few seconds seems sufficient for the development of inflammation.

1) Ikai,A., Nakamura,M. and Aoki,Y. (1989) Biochem. Biophys. Res. Commun. 158, 831-836.
2) Aoki,Y. (1978) J. Biol. Chem. 253,2026-2032.
3) Partridge,S.M., Davis, H.F. and Adair,G.S. (1955) Biochem. J. 61, 11-21.
4) Banga,I., Balò,J. and Horváth,M. (1959) Biochem. J. 71, 544-551.
5) Serafini-Fracassini,A., Field,J.M., Rodger,G. W. and Spina,M. (1975) Biochim. Biophys. Acta 386, 80-86.
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H. Arakawa, H. Tsuruta, Y. Amemiya, H. Kihara and A. Ikai

Kinetics of the Conformational Change of α_2-Macroglobulin Observed with X-Ray Solution Scattering and Fluorescence

The rates of gross conformational change of α_2-macroglobulin (α_2M) and ovomacroglobulin