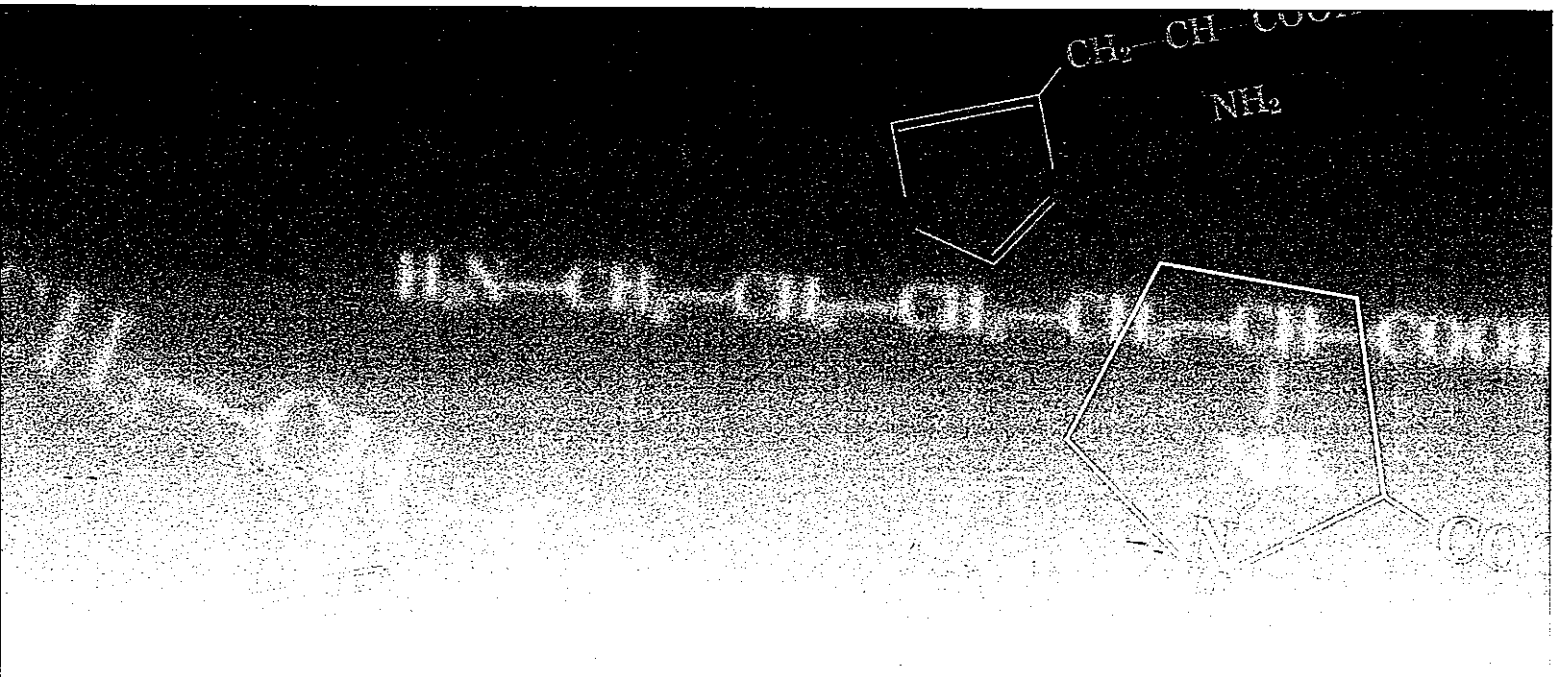

Pre Congress Symposium

Advances in Amino Acid Research in Human Health and Disease

Abstracts

Amino Acid Transporters in Cancer: Relevance to Its Diagnosis and Therapeutics

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Amino acid transporters are the essential cellular component for cells to grow and survive. They are regulated to keep up with the cellular metabolism so that living cells can take up amino acids depending on the metabolic requirements. In addition, the cells are equipped with the mechanisms to adapt their metabolic activity to the amino acid availability, which is critical for the cells to harmonize protein synthesis with amino acid supply and to prevent metabolic crisis and cell death.

In tumor cells, amino acid transporters are upregulated to support massive protein synthesis for continuous growth and proliferation. Among amino acid transporters expressed in tumor cells, system L transporters have been proposed to be crucial to supply tumor cells with large neutral amino acids including many essential amino acids. We previously identified an amino acid transporter designated LAT1 (L-type amino acid transporter 1) which subserves system L[1]. LAT1 is highly expressed in human malignant tumors including colorectal carcinomas, gastric cancers, pancreatic tumors, mammary gland carcinomas, renal carcinomas, esophageal carcinomas, lung cancers, prostate cancers and gliomas. In contrast, cells in normal tissues express the other isoform of system L transporter LAT2[2]. We have found that the high expression of LAT1 in tumors is correlated with poor prognosis in lung cancers, prostate cancers and colorectal carcinomas[3,4]. Thus, LAT1 can be a molecular target for the diagnosis of cancers. In fact, many radiolabeled amino acid probes have been used for bio-imaging and diagnosis of cancers. Among them we have found that ^{18}F-FMT (L-[3-^{18}F]-α-methyltyrosine) is selective for LAT1 and an excellent probe in positron emission tomography (PET) for the diagnosis of cancers[5,6]. Different from ^{18}F-FDG (^{18}F-fluoro-deoxy-glucose) conventionally used for PET diagnosis of cancers, ^{18}F-FMT is specific to cancers and not accumulated in non-cancerous legions. Additionally, ^{18}F-FMT can be applied to brain tumors because the brain background is low in ^{18}F-FMT PET.

Because LAT1 is upregulated in tumor cells to support continuous growth and proliferation, the inhibition of LAT1 is expected to suppress cancers. We have examined the effect of inhibition of LAT1 on tumor growth and found that a classical system L inhibitor, 2-aminobicyclo-(2,2,1)-heptane-2-carboxylic acid (BCH), and an antisense oligonucleotide designed against LAT1 inhibits the proliferation of tumor cells and suppressed the growth of tumors subcutaneously inoculated to nude mice. In agreement with this, the inhibition of LAT1 by BCH and the antisense oligonucleotide prolongs the survival of tumor-bearing mice. Therefore, it is proposed that the inhibition of LAT1 could be a new rationale to anti-tumor therapy.

In order to design the LAT1-specific high-affinity inhibitors, we examined the properties of substrate recognition by LAT1. We found that LAT1 relies on the ionic interaction with α-carboxyl group and α-amino group and on the hydrophobic interaction with a hydrophobic moiety of the substrates[7]. Based on this, we designed chemical compounds and obtained LAT1 inhibitors with an affinity ~1,000 fold higher that that of BCH. They effectively suppressed tumor growth in vivo and in vitro at lower doses compared with those for BCH. These newly developed high-affinity inhibitors would be useful for anti-cancer therapy in suppressing tumor growth with less affecting cells in normal tissues.

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Profile

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Sakamoto H, et al.: Biochem. J. 417:441-8 (2009).

Beyond Amino Acids: Quantifying Posttranslational Changes in Proteins in Nutrition and Physiology

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Heart failure results from the heart's inability to pump a sufficient amount of blood to meet the body's metabolic needs. In an adult human's heart, inadequate pumping is commonly attributed to left ventricular dysfunction due to abnormalities in cardiac structure, rhythm, and/or conduction. Heart failure is reaching epidemic proportions in the United States, affecting 4.8 million Americans and is a leading cause of hospitalization for people over 65 years of age. The 5-year survival rate is only 25% for men and 38% for women after diagnosis with a severe form of heart failure. Although the statistics appear bleak, advances in therapeutic treatment have improved the survival rate, and there is hope that understanding the underlying molecular defects in the failing heart will lead to future improvements in therapeutic treatment.

The progression of the symptoms of heart failure is highly correlated to a remodeling process within the heart that affects contractile function. This cardiac remodeling process involves changes in whole heart morphology as well as molecular alterations of both the contractile and calcium handling proteins. One of many potential alterations that occur during heart failure includes the phosphorylation of thin filament proteins. The thin filament proteins are directly involved with regulating the response of the contractile apparatus to calcium ions and, thus, are intimately involved with the regulation of heart contraction. Protein phosphorylation is known to modulate protein function in many biological systems. However, the mechanisms by which phosphorylation alter function are difficult to study due to the complexity of multiple phosphorylation events and a lack of simple molecular assays to identify and quantify protein phosphorylation. To this end, we developed a liquid chromatograph-mass spectrometry method for the identification and quantification of site-specific protein phosphorylation. The method is based upon standard proteomics approaches to identification of proteins based up peptide digests. This approach is applicable to study of protein phosphorylation and its regulation of both metabolic regulation and physiological function that is affected by nutritional changes.

The general method of proteomics and the specific method of identifying and quantifying site-specific protein phosphorylation will be discussed. An example will be given of measurements of human heart muscle biopsies in normal subjects and in heart-failure patients. We have observed a decrease in the phosphorylation of the thin filament regulatory protein, troponin I, during heart failure and identified and quantified a novel phosphorylation site located on the C-terminus of the thin filament regulatory protein, tropomyosin. These findings provide a direction for future research into the regulation of cardiac muscle contraction during heart failure.

Profile

■Education

B.A. - DePauw University, Greencastle, Indiana, May 1973.

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7/80 - 7/86	Research Assistant Professor of Medicine, Washington University School of Medicine, St. Louis, MO
7/86 - 6/96	Associate Professor of Biochemistry in Medicine, Cornell University Medical College, New York, NY
7/86 - 6/96	Director of the Mass Spectrometry Center in Medicine, Cornell University Medical College, New York, NY
7/87 - 6/96	Associate Professor of Biochemistry in Surgery, Cornell University Medical College, New York, NY
7/87 - 6/96	Director of the Core Laboratory of the Adult General Clinical Research Center, Cornell University Medical College, New York, NY
7/96 -	Professor of Medicine, College of Medicine, University of Vermont, Burlington, VT
7/96 -	Professor of Chemistry, College of Arts & Sciences, University of Vermont, Burlington, VT
7/96 -	Director of the Mass Spectrometry Facility of the Clinical Research Center, University of Vermont College of Medicine, Burlington, VT
7/02 -	Chairman, Department of Chemistry, College of Arts & Sciences, University of Vermont Burlington, VT
2/03 - 2/04	Ad hoc member, NIH Nutrition (NTN) Study Section
6/04 - 6/05	Ad hoc member, NIH Integrative Nutrition and Metabolic Processes (INMP) Study Section
2003 - 2005	Special Emphasis Panel/Review Group, NIH NCRR Shared-Instrument Grant Program
7/05 – 6/08	Member, NIH Integrative Nutrition and Metabolic Processes (INMP) Study Section
7/06 – 6/08	Chair, NIH Integrative Nutrition and Metabolic Processes (INMP) Study Section
9/07	Member, Vermont Academy of Science and Engineering

■Professional Memberships

American Chemical Society (ACS) 1975

American Physiological Society (APS) 1989

American Society for Biochemistry & Molecular Biology (ASBMB) 2002

American Society for Mass Spectrometry (ASMS) 1975

American Society for Nutrition (ASN) reorganized in 2006 from 1984

American Society for Clinical Nutrition (ASCN)

American Society for Nutritional Sciences (ASNS, formerly the Am. Inst. of Nutrition, AIN)

Potential Use of Amino Acids in Identifying Nutritional and Disease States

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The association between certain disease states and abnormalities in plasma levels of some metabolites including amino acids, have been noted in the past. There are few studies, however, on the use of metabolic profiling of amino acids to reveal underlying physiological states and to discriminate between specific diseases. We report here the development of novel methods to analyze how certain physiological states affect the relationships between the various plasma amino acid levels and to generate indices based on plasma amino acid levels to discriminate between various physiological and disease states.

In 2003, we showed that cluster analysis of multivariate correlations of all plasma amino acid levels allowed the visualization of relationships between plasma amino acid levels[1], while in 2006 we showed that network analysis of plasma amino acid levels and tissue amino acid levels indicated that data-driven networks for blood and tissue could be constructed[2]. We have also applied this analysis to quantitative gene expression data for numerous metabolism genes obtained by RT-PCR of the same tissues that were used for amino acid measurements to generate gene expression networks for low and high protein states[3]. We believe that using this type of correlation based analysis, it may be possible to analyze certain types of "-omics" data together to obtain data-driven structures.

Using plasma amino acid data from various disease model rats, we showed that by using a novel computer based method, we could derive a diagnostic index composed of plasma amino acid levels(AminoIndex®) to distinguish a particular disease model from another[2]. The AminoIndex® is a summed ratio type expression and is given by a computer program that calculates the expression, among the many possible combinations, that gives the best correlation with the target parameter. Discontinuous or continuous data can be handled and in the latter case surrogate markers for difficult to obtain biological parameters could be produced, while in the former case an AminoIndex® to separate physiological or disease states could be obtained. We have applied the AminoIndex® to clinical data and after overcoming technical problems such as amino acid degradation during blood handling, preliminary results suggest that AminoIndex® can be generated to distinguish a number of different clinical conditions in humans.

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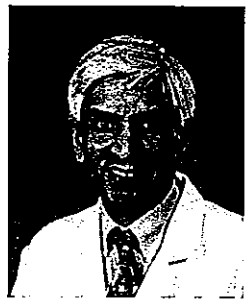
Profile

Takeshi Kimura studied Cell and Molecular Biology at University of London, King's College and obtained a PhD in Biochemistry from University of London in 1984.
He was Visiting Fellow and Visiting Associate at the National Institutes of Health in the USA from 1984 to 1989. In 1989 he joined Ajinomoto and worked at the Central Research Laboratories and External Scientific Affairs department at head office. He then served as head of the Washington DC Office from 1992 to 1997. In 1998 he started the Basic Safety Research Group at the Institute of Life Sciences. From 2005 till present he is General Manager of Quality Assurance and External Scientific Affairs Department. He has been nominated to become Corporate Executive Officer. He is also Chief Executive Officer for the International Glutamate Technical Committee, Chief Executive Officer for International Council on Amino Acid Science and President of Food and Health Forum.

Advances in Amino Acid Metabolism in Human Infants



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Nutritional management of newborn infants born at term gestation and those born prematurely continues to be a challenge in spite of major advances over many years. This is particularly important for the premature infants, since several clinical studies have consistently shown that, in spite of our best efforts, a large proportion of prematurely born infants are growth restricted at term gestation. Thus with the goal of providing optimal care, a number of groups have examined systemic amino acid metabolism, splanchnic amino acid uptake, and have estimated individual amino acid requirements for these infant using isotopic tracer methods. In this review, some of the recent developments in our understanding of the amino acid metabolism in the newborn are presented.

Intravenous amino acid infusion in preterm infants causes a suppression of whole-body rate of protein breakdown[1]. Such an effect is, however, transient and reverts to the basal state if the amino acid infusion is continued. The excess amino acids are disposed of via oxidation and urea synthesis. Supplementation of the parenteral amino acids with glutamine sustained the suppressive effect of amino acids on protein breakdown after 3-5 days[2]. Data from studies in adults also show that amino acids induce only a transient increase in protein synthesis in the skeletal muscle. The mechanism of the transient responses, and the specific tissue compartment involved are unclear. However, these observations may have important clinical implications for amino acid administration and may provide a rationale for intermittent change in dosage rather than a constant dose/rate infusion.

Glutamine, a non essential amino acid, is important for a number of physiological functions and has been described as conditionally essential during "acute stress". It has been suggested that during acute illness, the demand for glutamine outweighs its rate of synthesis. Data in newborn infants show that the rate of glutamine synthesis can be increased by intravenous infusion of its carbon precursors[2]. As in adults, glutamine metabolism in the neonate is compartmentalized between the splanchnic tissues and the periphery. Enterally administered glutamine is entirely metabolized in the splanchnic compartment and does not appear in the systemic circulation. Therefore enterally administered glutamine will have its primary effect on the splanchnic tissues, i.e. gut, its barrier function, mucosal immunity, etc. By contrast, parenterally administered glutamine may have its major impact on peripheral tissues such as its effect on protein metabolism in skeletal muscle.

Studies of methionine kinetics show that transmethylation rates are high in both full term and preterm infants[3]. In addition, transsulfuration of methionine is evident in the immediate newborn period. This is important since activity of enzymes involved in transsulfuration is low or absent in the fetal liver. These data suggest that cysteine may not be considered "essential" for the neonate. The high rate of transmethylation may be related to high methylation demands at this stage in development, while high transsulfuration may be aimed at meeting high demands for glutathione.

Other research investigations have documented the high metabolic activity of the splanchnic compartment as evidenced by high rate of metabolism and first pass uptake of several enterally administered amino acids[4,5].

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Profile

Satish Kalhan, M.D. is Staff in the Departments of Pathobiology, and Gastroenterology, Hepatology Cleveland Clinic, and Professor in the Department of Medicine, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University. Prior to joining Cleveland Clinic, he worked at MetroHealth Medical Center and Rainbow Babies and Children's Hospital.

Satish Kalhan received his medical degree from All India Institute of Medical Science in New Delhi, India. He then moved to the UK where he received training in medicine and pediatrics in Leeds, Sheffield and London, and received the post graduate degree (MRCP) from the Royal College of Physicians, UK.

In 1970, he moved to Cleveland to then Cleveland Metropolitan General Hospital / Case Western Reserve University. He has remained here ever since and worked in all the three major institutions. Starting as a junior faculty member at Case Western Reserve University, he has moved through the ranks to be appointed as tenured Professor in the Department of Pediatrics in 1986 and in the Department of Reproductive Biology, and now in Medicine.

He has served on numerous local and national advisory committees, NIH advisory groups, and has received a number of awards and honors. He has published over 200 original articles, book chapters and reviews, and has trained a number of students and fellows. He is a member of several professional societies and serves or has served on the editorial board of a number of respected peer reviewed journals.

His research career started after his arrival in Cleveland when he became interested in the clinical problem of hypoglycemia in the infants of diabetic mothers. In order to examine the mechanism of low blood glucose in these babies, he, in collaboration with Sam Savin PhD of the CWRU Department of Geology, developed the analytical methods to use safe, non-radioactive, stable isotopic tracers of glucose. This was the first time that such a technology was developed and used in perinatal medicine. He has been continuously supported by grants from the National Institutes of Health for over 30 years.

Satish Kalhan's research has been focused primarily on whole body metabolism in man and its perturbations as a consequence of diabetes and related disease states. Being a neonatologist by clinical training and practice, he has had special interest in the mother, fetus and the newborn infant. In this context, he and his colleagues have made major contributions to the understanding and management of alterations in the mother's metabolism as a result of diabetes in pregnancy, and its consequences to the fetus and newborn infant. In addition, they have made significant contributions to the study of amino acid kinetics and metabolism in the neonate and have developed nutritional intervention strategies for the care of the prematurely born infant. All of this work has involved the use of sophisticated, complex, non-radioactive tracer methodologies in combination with mass spectrometry. Because of the safety of their approach, these complex techniques could be employed not only in the smallest of prematurely born babies, but also in adults and pregnant women.

More recently, Dr. Kalhan and his colleagues have focused their work on the mechanism of accretion of fat and the pathogenesis of fatty liver disease in obesity in humans.

Advances in Amino Acid Metabolism and Requirements in the Aging Human

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The requirements for protein across the lifespan have been studied for decades, but recommendations for adequate intake have always stimulated debate. Recently, protein intakes above the Recommended Dietary Allowances have been touted to be beneficial for some individuals, especially the elderly population. However, there remain gaps in our knowledge about the optimum intake of protein and specific amino acids for older individuals, especially when taking into consideration age-associated changes related to sarcopenia, osteoporosis, immune function and risk for diabetes mellitus. Moreover, there is global concern in terms of the growing population of elders, the production and availability of food, food insecurity and the environment, all of which can impact the adequacy of nutrient intake.

Epidemiological studies support a positive relationship between dietary protein intake and bone and muscle mass. However, with the high prevalence of obesity, diabetes mellitus, cancer and cardiovascular disease worldwide, recommendations have been made to move towards more plant-based diets, which have been associated with a lower risk for these disorders. Alterations in the source of dietary protein may influence the intake of specific amino acids, which may in turn influence cellular processes important in advancing age. Key amino acids include leucine, methionine, cysteine, arginine and glutamine. New information in the context of protein and amino acid requirements in the aging human will include the safety and efficacy of high protein diets, the balance between plant- and animal-based protein for optimal health, and the interactions between diet and physical activity.

Profile

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Chief Residency (1978-79) University of Vermont, Burlington, VT
Nutrition/Gastroenterology Fellowship (1981-85) Harvard Medical School, Children's Hospital, Boston, MA
Post-doctoral Associate (1985-87) MIT; Research Fellow in Medicine, Beth Israel Hospital, Boston, MA

Dr. Fukagawa began her research career by applying nutritional biochemistry, metabolism, stable isotope technology, and mass spectroscopy to clinical research. The focus of her thesis was on insulin resistance and the regulation of protein metabolism in aging humans. She has had continuous external grant support and her work remains focused on physiologic and nutritional changes associated with aging, specifically the sulfur amino acids, methionine, cysteine, and homocysteine and the tripeptide, glutathione, one of the major endogenous antioxidants. Despite her commitment to and expertise in clinical investigation, Dr. Fukagawa recognized the need to couple a more reductionist approach to bridge the bench with the bedside. Hence, while at Rockefeller University, she began "retooling" in molecular and cell biology. At UVM, she continues her work on age- and diabetes-related disorders in human volunteers on the GCRC but also focuses on oxidative stress, age- and glycemia-related effects on transcription factor activation (NF-κB and AP-1), mitochondrial function and the regulation of glutathione synthesis in vascular smooth muscle cells. Dr. Fukagawa also recently began investigating the link between inhaled pathogenic fibers and cardiovascular disease in an animal model of atherosclerosis using the Votey Inhalation Facility.

Dr. Fukagawa has served on numerous NIH review panels and served as the Chairman of the NIH study section for GCRC's. She currently serves on the NIH Integrated Physiology of Obesity and Diabetes Study Section. Dr. Fukagawa was President of the American Society for Clinical Nutrition (American Society for Nutrition) and now serves as an Associate Editor for the American Journal of Clinical Nutrition.

■Recent Representative Publications:
Fukagawa NK, Martin JM, Wurthmann A, Prue A, Ebenstein D, O'Rourke B. Sex-related differences in methionine metabolism and homocysteine concentrations. Am J Clin Nutr 2000;72:22-29.

Li M, Liu RM, Timblin CR, Meyer SG, Mossman BT, Fukagawa NK. Age affects ERK1/2 and NRF2 signaling in the regulation of GCLC expression. J Cellular Physiol 2006; 206:518-525.

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Jez JM, Fukagawa NK. Plant sulfur compounds and human health. In: Sulfur: A Missing Link Between Soils, Crops, and Nutrition. 2007.

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Advances in Amino Acid Metabolism in the Injured Human

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Metabolic regulation in the injured or septic individual is different from that in healthy individuals. Protein and amino acid metabolism is regulated to meet different priorities in injury/sepsis as compared to the healthy state. This applies to the basal non-fed state as well as the fed state. The basic energy fuel is fat for both health and injury/sepsis, but the priority to endogenously produce sufficient amounts of glucose is much stronger in injury. In an healthy individual provision of exogenous glucose immediately inhibits gluconeogenesis, which is not the case in injury/sepsis. On the opposite gluconeogenesis is very difficult to supress in an injured individual. To feed the gluconeogenetic pathway with substrates, a surplus of free amino acids is needed. This susrplus comes from a constant dominance of protein degradation over de novo synthesis. In most cases both de novo synthesis and degradation of proteins are elevated in injury/sepsis, but degradatin to a greater extent than synthesis. In healthy man this is similar to the non-fed state, but in injury/sepsis food intake will not alter the dominance of degradation over synthesis. The regulation described here is on a whole body basis, but may not be true in individual tissues such as the liver and in immune cells. In particular the dominance of degradation over synthesis is true for skeletal muscle, which very rapidly becomes depleted in injury/sepsis[1]. To some extent this depletion may be related to inactivity, but to a larger extent this is driven to be the metabolic re-regulation outlined above.

Beside the function as brick-stones in proteins, the individual aminos acids are involved in other metabolic pathways. Into energy metabolism, where the carbon skeletons of most amino acids are used in gluconeogenesis after de-amination of the amino groups. Therefore there is a considerable interchange of amino acids within the cells as well as in-between cells and tissues. A great deal is known of this interchange through studies of inter-organ amino acis transport as well as through studies of isotopically labelled amino acids to disclose the metabolic pathways. In muscle there is an export of all amino acids except for glutamate in the basal state of health and in injury/sepsis[2]. This is a similarity in qualitative terms, but quantitatively the export is manyfold larger in injury/sepsis. Furthermore the proportions between the individual amino acids in this export do not reflect the amino acid composition of muscle proteins. Instead alanine and glutamine are heavily overrepresented, and these two amino acids corresponds to 2/3 of the total amino acid export. In the fed state this export is converted into a net uptake of all amino acids across muscle tissue in healthy individuals. This net uptake goes for all amino acids except for glutamine, which is constantly exported from muscle. In injury/sepsis feeding does not alter the export of amino acids from muscle in quantitative terms, although the depletion of muscle proteins is to some extent attenuated.

The net result of this inter-organ exchange of amino acids in man is a constant endogenous de novo production of glutamine, which corresponds to approximately 60 g / 24h[3,4]. The production rate is similar in health and injury/sepsis. The major part of the endogenously produced glutamine is used as energy substrate in rapidly dividing cells, such as enterocytes and immune cells, which are mainly located in the splanchnic area. Glutamine is a fairly good energy substrate,but it carries an energetic cost in terms of handling the two amino groups that are contained in glutamine.The rationale for this metabolic pathway of glutamine is suggested to be a guaranty for nucleotide production, which uses glutamine as a precursor.

In the rapidly dividing cells a surplus of glutamine will make it possible to increase nucleotide production, perhapes 100-fold, very rapidly if needed. In injury/sepsis the demand for cell dicision and protein synthesis in these cell populations becomes increased, hence the need for the nucleotide precursor glutamine increases. The endogenous glutamine production may in these situations become insufficient, and as a result depletion of free glutamine in plasma and in tissues is seen following injury/sepsis[1]. Individuals with a low plasma glutamine concentration has a worse outcome and more complications[5].

It has been suggested that supplementation of exogenous glutamine to restore plasma glutamine concentration may improve outcome in injury/sepsis. So far it has been demonstrated that supply of exogenous glutamine can restore plasma glutamine concentration back to normal[6], and that mortality/morbidity of ICU patients given such supplelmetation is improved[7]. So far the mortality benefit has only been demonstrated for ICU patients on parenteral nutrition. Presently several multi-center studies over glutamine supplementation are in progress and several additional mechanisms of action are suggested. The present level of evidence is to recommend exogenous glutamine supplementation to ICU patients requiring parenteral nutrition. For patients on enteral nutrition the evidence is more controversial, but new studies are in the pipe-line.

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Profile

■Education

1974 Graduate in medicine
1977 Bachelor of medicine
1979 M.D. licensed doctor
1983 Specialist in Anaesthesiology & Intensive Care Medicine
1985 Ph.D. Anaesthesiology & Intensive Care Medicine
Ass Prof of Anaesthesiology & Intensive Care Medicine
Professor of Anaesthesiology & Intensive Care Medicine

■Academic credentials

Head supervisor of 12 PhD students
> 200 original publications

■Former appointments

Chairman at the Department of the Anaesthesiology and Intensive Care Unit, Huddinge University Hospital 1994-2000
Chairman at the Department of the Anaesthesiology and Intensive Care Unit, St Görans's Hospital Stockholm 1990-1994
Director Department of Intensive Care, Huddinge University Hospital 1987-1990
Chairman ESPEN Scientific Committee 1995-1998
Member of ESPEN Scientific Committee 1992-1995
Chairman of the Working Group for Intensive Care in the Swedish Society for Anaesthesiology & Intensive Care 1995-1998.
Director for the Division of Anesthesiology in the KARO Institution, Karolinsksa Institutet 1994-2001
Swedish representative in the ESICM Council 2000-2002

■Present appointments

Professor of Anaesthesiology and Intensive Care at Karolinska Institutet since 2000
Director of the Unit of Anaesthesiologic Metabolism at the Clinical Research Centre, Karolinska University Hospital, Huddinge at Karolinska Institutet, Stockholm since 1995.
Member of the Steering Group for Post-graduate Intensivist training in Scandinavia since 1998, and member of the Advisory Board for the Scandinavian Critical Care Trails Group since 2002.
President of the Swedish Association for Anesthesia and Intensive Care Medicine (SFAI) since 2007
Member of the ESICM Executive Committee and Treasurer of the society 2002-2007
Associate Editor of Acta Anaesthesiologica Scandinavia since 1998
Associate Editor of Intensive Care Medicine since 2007
Member of the Editorial Boards of Clinical Nutrition, Journal of Parenteral and Enteral Nutrition, Current Opinion in Clinical Nutrition and Metabolic Care and Nutrition.