

PERSONALIZED NUTRITION AND MEDICINE IN PERINATAL DEVELOPMENT KAPUT, CHEN, SLIKKER JR. pdf

1: Teratology Society Meeting

Contents: Role of apoptosis in normal and abnormal development / Philip Mirkes -- Signal transduction pathways as targets for teratogens / Barbara www.enganchecubano.com -- Nutrition in developmental toxicology / Deborah K. Hansen -- Epigenetic mechanisms: role of DNA methylation, histone modifications, and imprinting / Robert G. Ellis-Hutchings and John M.

Boctor , Cheng Wang , and Sherry A. Received May 2; Accepted Jul Copyright Published by Oxford University Press This article has been cited by other articles in PMC. Abstract Treatment with N-methyl-D-aspartate NMDA receptor antagonists, such as ketamine KET or phencyclidine PCP , can trigger apoptotic neurodegeneration in neonatal rodents; however, little is known about the behavioral alterations resulting from such treatment. Postinjection, the home cage behavior of each pup was categorized on PNDs 7–11. Slant board and forelimb hang behaviors were examined on PNDs 8–11 and 12–16, respectively. PCP treatment caused substantial abnormal home cage activity on each injection day PNDs 7, 9, and 11. These data indicate that developmental NMDA antagonist treatment causes short-term behavioral alterations which appear related to motor coordination and may be cerebellar in nature. Such NMDA antagonist-induced neurodegeneration has been shown to result in behavioral deficits as well. For example, neonatal PCP or MK treatment causes later sensorimotor gating deficits as measured by prepulse inhibition Harris et al. Neonatal PCP treatment has been described to cause increased sensitivity to later PCP treatment as well as transient deficits in spatial alternation performance Wang et al. Repeated neonatal MK treatment results in long-term deficits in radial-arm maze performance Kawabe et al. Those behavioral deficits imply that the observed neurodegeneration following developmental NMDA antagonist treatment has long-term effects. The description of long-term behavioral effects after developmental NMDA antagonist treatment led us to hypothesize that there may be acute effects observable during treatment. Here, the behavioral effects of PCP or KET were evaluated using those treatment regimens previously shown to produce significant neurodegeneration. As a preliminary exploration, the potential protective effects of L-carnitine were measured in KET-treated rats since L-carnitine appears to prevent glutamate neurotoxicity Felipo et al. Home cage behavior of the pups was rated using a comprehensive scoring system on PNDs 7–11 after each treatment. Slant board negative geotaxis; PNDs 8–11 and forelimb hang PNDs 12–16 behaviors were examined to assess potential early neurotoxicant-induced dysfunctions. Each dam was individually housed in a standard polycarbonate cage lined with wood chip bedding and provided with ad libitum food NIH, Purina Mills, St Louis, MO and water. Each pup was paw tattooed on PND 1 and also identified with a nontoxic marker on the dorsal side and tail tip on PND 4. Solutions were made weekly and kept refrigerated. The sc injections were done using a gauge needle. Thus, similar to that described by Zissen et al. However, as noted by Zissen et al. Treatment assignment was based on PND 4 body weight such that all groups had similar average body weights prior to treatment. The doses and treatment regimens were based on previous reports indicating that similar treatments caused neurodegeneration in rats Ikonomidou et al. The L-carnitine dose was based on studies of its protective effects against 1-methyl-phenylpyridinium ion-induced apoptosis Wang et al. On PNDs 8–11, body weights were recorded after behavioral testing and prior to treatment. At each treatment time, the dam was placed in a holding cage. Each pup was then identified and when indicated, injected. Those pups not injected e. Time from dam removal to replacement into the home cage was less than s. At 5, 14, 23, and 32 min posttreatment, the behavior of each pup was assessed by one of two experimenters blind to treatment. Thus, there were four observations at five of the six treatment times on PND 7 i. On PNDs 8–11, there were four observations following the Each pup was categorized as exhibiting one of 12 different behaviors see Table 1 which were based on a previous scoring system Goodwin and Barr,

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2: Translational genomics - Europe PMC Article - Europe PMC

Personalized Nutrition and Medicine in Perinatal Development Personalized Nutrition and Medicine in Perinatal Development. By Jim Kaput, James J. Chen, and.

The pharmacologic and toxic effects of drugs on the mother, placenta, and the fetus are governed by a complex but integrated set of variables consisting of mother, uterus, placenta, amniotic fluid, and fetus. A number of variables can modify the intensity and duration of pharmacologic effect: Factors that determine the rate and the percentage of the compound that is absorbed bioavailability are the physiochemical characteristics of the drug, its rate of dissolution, the gastric and intestinal pH, gastric emptying time, composition of intestinal contents, intestinal motility, and mesenteric blood flow. After absorption, drugs enter the intravascular system and either circulate in free form or are bound to plasma proteins to differing degrees depending on their binding characteristics and other competing ligands. Distribution of unbound drugs throughout the body is frequently a rapid process that allows diffusion equilibrium to be quickly established between blood and other body compartments. In some situations, however, the access of a drug to the sites of its pharmacologic action may require considerable time. Among other factors, drug distribution is influenced by lipid solubility, degree of ionization, blood flow, and binding affinities to proteins in plasma and specific tissues. Although renal excretion of unchanged drugs is by far the most important excretory route, there are several other excretory pathways such as biliary excretion or alveolar elimination used by certain compounds. These excretory pathways may assume greater importance in certain pathologic conditions that preclude the use of the primary excretory route. These differences are important not only for maternal therapy but also for understanding the effects of fetal drug exposure, and potential fetal therapeutics. Role of gender The effects of the pregnant state on the disposition and action of drugs are superimposed on the changes associated with the female sex. Sex differences regarding drug disposition in experimental animals have been known for more than 60 years, but it was not until that the FDA encouraged the inclusion of women in clinical trials. Physiologic differences between the sexes may explain variations in the absorption of drugs. Compared to men, women have slower gastric emptying time and prolonged colonic transit time. These differences may be heightened during pregnancy. There are also differences in drug biotransformation. A multienzyme system is responsible for the degradation of hydrophobic molecules. In a sequential manner, hydrophobic molecules are biotransformed by phase I enzymes and then conjugated by phase II enzymes to produce water-soluble products. These enzymes are expressed mostly in the liver but also to a lesser extent in other tissues e. The expression pattern of different CYP isoforms differs between the sexes. Other drugs, such as diazepam, caffeine, and some anticonvulsants, metabolized by CYP2C19 or CYP1A2 appear to be metabolized faster in men than in women. Sex differences in the receptors and transporters have not been systematically studied. Studies in animal models have shown sex differences but the results have not been validated in human studies. There are also sex differences in the sensitivity to drugs. For example, drug-induced torsades des pointes and the cough induced by angiotensin-converting enzyme inhibitors occur more commonly in women. Similarly the influence of genetics remains to be determined. The amount and rate of transfer of drugs to the fetus determine the presence or absence of pharmacologic or toxic effects. With the rare exception of drugs injected directly into the fetal compartment, the path a drug must take from its administration to the mother is across the maternal organism to its site of action in the fetus. This multicompartiment system is especially complicated because it does not represent a constant relationship but one that is continuously changing throughout pregnancy Fig. Pathway and factors affecting xenobiotic disposition by mother and fetus. Reports in the literature suggest that a generalized malabsorption state may be induced or exacerbated during pregnancy. There is also indirect evidence that absorption of certain compounds such as digitoxin, salicylamide, and phenytoin may be delayed in pregnant patients. For example, the increased residence time due to the decrease in intestinal motility could lead to a decreased bioavailability because of an increase in gut

metabolism. The complexities of performing bioavailability studies in pregnancy can be simplified with the use of stable isotopes. The intravenous injection of a stable isotope-labeled drug coupled with the concomitant oral administration of unlabeled drug permits the simultaneous determination of both drug profiles and therefore minimizes the variability associated with two separate studies. These adjustments can be expected to be more influential toward the end of pregnancy. Indeed, the absorption rate of meperidine after intramuscular administration has been found to be slower in women during labor than in nonpregnant controls. Distribution

The remarkable changes in the volume of water and composition of body compartments, coupled with the hemodynamic adjustments that occur during pregnancy, set a background for drug distribution that is quite different from that present in nonpregnant persons. Dilutional hypoalbuminemia, especially in the last trimester, is mainly responsible for a decrease in drug-binding capacity and a consequent increase in body distribution. The great interindividual variability in the distribution of drugs such as meperidine given during labor may be attributed to variations in the hemodynamic makeup of different women. Hepatic blood flow measured in absolute terms does not appear to be altered during pregnancy. Proportionally, however, the percentage of cardiac blood flow reaching the liver is decreased. Clinical studies using metabolic probes have shown that CYP1A2, xanthine oxidase, and N-acetyltransferase activities are decreased, but CYP3A4 is increased during pregnancy. Dosages of drugs predominantly metabolized by these isoenzymes may need to be increased during pregnancy in order to avoid loss of efficacy. In contrast, CYP1A2 and CYP2C19 activity is decreased during pregnancy, suggesting that dosage reductions may be needed to minimize potential toxicity of their substrates. Current knowledge is based primarily on observational studies, many including small numbers of women. For some isoenzymes, the effect of pregnancy on only one drug has been evaluated. The full-time course of pharmacokinetic changes during pregnancy is often not studied sequentially during pregnancy. In both homozygous and heterozygous fast metabolizers, CYP2D6 activity increased, whereas the activity of this polygenic enzyme decreased in homozygous poor metabolizers. The reported increase in plasma clearance of phenytoin and phenobarbital during pregnancy has been attributed to an increase in metabolic rate. Glucuronidation of salicylamide has been found to be depressed in parturients. There is indirect evidence, however, of increased glucuronidation of other substrates, such as zidovudine. UGT1A1 and UGT2B7 have been identified as the enzymes producing labetalol glucuronides possibly under the modulating influence of progesterone. The profound changes in function are likely to affect the renal excretion of drugs. The increase in glomerular filtration observed during pregnancy is counterbalanced to a significant extent by modifications in tubular reabsorptive capacity. Of greatest importance from the pharmacokinetic standpoint are diurnal variations in function. Although for the purpose of this discussion, absorption, distribution, and elimination of drugs in the maternal organism have been considered separately, the interplay among these factors determines the time course of maternal plasma levels. Little is known about the extent to which complications of pregnancy modify drug disposition in the mother. However, recent work has uncovered a bewildering number of complex functions affecting both maternal and fetal physiology. The three major factors affecting drug transfer across the placenta are physiochemical characteristics of the compound, pharmacologic properties of the placental tissue, and maternal and fetal placental blood flow. Physiochemical characteristics include molecular weight, lipid solubility, degree of ionization, molecular configuration, and tissue protein properties. Generally, lipophilic substances and compounds with low molecular weight tend to diffuse rapidly into the fetal circulation. Poorly ionized drugs at physiologic pH, such as thiopental, reach the fetal circulation quite rapidly. Certain compounds, such as the sympathomimetic agents, salbutamol, ritodrine, and norepinephrine, appear to have a low transfer rate despite their small molecular weights. Still, sufficient amounts of both salbutamol and ritodrine are transferred to produce fetal tachycardia. The purported placental impermeability to polar compounds is relative rather than absolute. Xenobiotics cross the placenta by different transfer mechanisms: The metabolic conversion by the placenta of one compound into another compound that in turn may be transferred cannot be discounted. Most drugs cross the placenta by simple diffusion at a rate that is directly related to the difference between the maternal and fetal blood concentrations.

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Recent studies have shown that the syncytiotrophoblast expresses membrane proteins that act as drug transporters. P-glycoprotein, an ATP-dependent drug efflux pump, is present in the brush border of the syncytiotrophoblast. A wide variety of drugs are substrates for this transporter. Transporters in the opposite direction have not been sufficiently characterized. Transporters, including organic anion transporter OATP, serotonin transporter, norepinephrine transporter NET, and several organic transporters are also expressed in the placenta, but their pharmacologic role remains unknown. The role of the carnitine transporter is in the delivery of carnitine to the fetus, however, a number of pharmacologic active compounds such as verapamil and cephaloridine may utilize this transporter. Bile acid transporters are present in the placenta and may be important in the efflux of compounds back into the maternal circulation. The physiologic role of placental nucleoside transporters ENT 1 and 2 is to facilitate the transport of purine and pyrimidine nucleosides from the mother to the fetus. A significant number of drugs including anticancer drugs may utilize these transport systems. There are transport systems in animal studies for which no endogenous substrates have been identified. Studies in the pregnant rodent seem to indicate that drug transfer is lowest in midgestation and peaks at the beginning and end of pregnancy. The relative maternal and fetal blood flow through the placenta is of paramount importance in determining the rate of drug transfer from mother to fetus and vice versa. Adequate measurements of uterine blood flow are flawed by technical difficulties. Despite this, several studies have shown an increase in uterine flow per kilogram of uterine weight toward term. When data are analyzed in terms of uterine blood flow per kilogram of fetus, however, a decrease is demonstrated at term. The typical time course of uterine and fetal plasma concentrations usually follows the pattern: Establishment of a maternal-fetal concentration gradient; Equilibration phase, in which the highest fetal drug concentration will depend on the placental factors discussed above; Fetal drug elimination phase. During this period, the combined effects of maternal drug biodegradation and elimination lower maternal drug concentrations, creating a fetal-maternal gradient and reversing the direction of drug transfer across the placenta. Delivery can occur at any point during this sequential pattern, and its timing will determine the amount of drug present and the ability of the newborn to handle xenobiotics. Many factors can influence maternal and fetal hemodynamics, thereby disturbing maternal and fetal drug distribution. Those affecting maternal hemodynamics are briefly reviewed here. A decrease in uteroplacental blood flow may be secondary to vasoconstriction of myometrial arterioles or obstruction of uterine venous outflow. The amount of drug transfer to the fetus, especially after a single intravenous pulse injection, will vary depending on the type of blood flow obstruction and the temporal relationship between drug administration and the onset of uterine hypoperfusion. For drugs given before the onset of uterine blood flow obstruction, myometrial arteriole vasoconstriction will tend to protect the fetus, whereas venous obstruction, by allowing a longer period of placental residency time, will result in increased fetal drug extraction. Alterations in uterine blood flow of particular interest are those related to abnormal labor, excessive uterine activity spontaneous or oxytocin-induced, vasoactive drugs, or vena cava compression and supine hypotension, as may occur at the time of removal of amniotic fluid. Pathophysiologic conditions, such as preeclampsia, hypertension, and diabetes, which may be associated with impaired uteroplacental blood flow, can be expected to decrease drug transfer across the placenta. On the other hand, these pathophysiologic conditions often are associated with profound fetal hemodynamic changes that favor drug distribution to the fetal brain. The demonstration that the human placenta is capable of metabolizing xenobiotics spurred a burst of investigative activity. Placental CYP1A1 is inducible by maternal smoking. The balance of present evidence, however, refutes this contention and supports the existence of separate P species of isoenzymes for the catalysis of xenobiotic and steroidal hydroxylation reactions.

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3: Garry R Cutting " Network " Johns Hopkins University

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This article has been cited by other articles in PMC. We therefore argue here basic science to be challenged and leveraged for its relevance to human health and societal benefits. This more recent approach and attitude are catalyzed by four trends or developments: Introduction Translational genomics is both the title and mission of this new journal. Translational research has a long history of practice that was formalized by the creation of the U. Governments throughout the world are funding research programs and centers e. The goals of these initiatives are to decrease failure rates, expenses, and timelines for drug and evidence-based product and solution development. In parallel with these government-funded programs, the U. This more recent approach and emerging scientific attitude root in four developments that we will outline hereunder: The increasing need for evidenced-based solutions The increasing prevalence of complex, age-related chronic diseases in developing and emerging economies is intensifying scientific, ethical and economic calls to improve the healthcare system Callahan, and act on related health disparities Dankwa-Mullan et al. The burden is intense for the genomics field, which over promised rapid solutions to disease from leveraging data from the Human Genome Consortium, N. G. , Venter et al. High-throughput laboratory and clinical data generation The second development reinforcing the concept that basic research can be translatable is the ongoing evolution in the ability to quantify physiologies and genetic makeups of large numbers of study participants and patients using omics-based and imaging technologies. In many cases, omic analysis is done with untargeted methods in a high-throughput screen e. NMR-based metabonomics, or MS-based proteomics , which is then followed by more targeted and hence more sensitive methods focusing on a subset of molecules. Targeted quantification requires specific method development, in contrast to the generic screening methods. Such hypothesis-limited Editorial, approaches differ from assessing a specific research question by means of measuring selected molecular readouts but promise to provide more comprehensive understanding of biological processes thanks to conceptually unbiased analysis Kaput and Morine, These omics sciences have evolved over the last few decades and are prime examples of how technology has transformed and driven biomedical and other areas of biology research. In almost all cases however, omics databases provide information about population averages or ranges for a molecule in a biofluid e. In many such cases, these ranges are specific to the tested population since not all or even many ancestral genetic makeups have been sampled. Omics data obtained from analyzing one person has demonstrated the long-known facts of biochemical and genetic individuality Williams, The growing self-quantification movement and several citizen science research projects are disrupting the population average database model since individuals are now sharing n-of-1 data, including genomic information. This open genome and personal data access movement started with the Personal Genome Project at Harvard, which sequenced and allowed access to the genomes of 10 individuals Church, , Lunshof et al. FDA has restricted these and other companies from providing associations to trait, phenotype, or disease Green and Farahany, , no restrictions were placed on the right of individuals to own their personal data Angrist, Hence, individuals can and do share their data. Associating individual genetic variants with complex phenotypes is less than robust Ransohoff and Khoury, mitigating present-day concerns about the potential for discriminatory use of genomic data, However, ongoing research increasingly associates patterns of gene variants with susceptibilities to diseases and traits and privacy concerns are likely justified. Access to individual genomic data holds great promise for making these associations. However, among the limiting factors for analyzing genetic data and outcomes is the lack of reliable and standardized dietary and lifestyle data, plus the missing access to personal omics data. Web-enabled research tools that capture, manage, store, and retrieve these personal molecular phenotype and lifestyle data are unavailable to the research community

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Stumbo et al. However, the true strength of NRC will come from aggregating individual data with data from other members of the cohort Monteiro et al. The smartphone revolution is being used by NRC and other initiatives since at least apps from [http: Healthcare](http://Healthcare) Boulos et al. Data harmonization Lynn et al. System thinking and analysis Modern biomedical research relies on very detailed mapping of biochemical reactions and interactions e. Despite their utility for mechanistic research, biological outcomes can usually not be predicted from this knowledge base. Metabolism and its regulation form a complex interacting set of processes that change over time and in different environments. System thinking and computational methods are now being increasingly used to help analyze and visualize biological systems such as endocrine, circulatory, digestive, nervous, and immune functions as well as response to vaccines Afacan et al. Modern system concepts e. Many of these system biology definitions and experimental approaches, however, miss the crucial inclusion of measuring environmental factors such as diet, psycho-social factors, physical activity, and other lifestyle factors, each of which may influence expression of genes, levels of proteins and metabolites Kussmann et al. The human body is not a closed system as demonstrated by changes in blood concentrations of one-carbon metabolites and cofactors as a consequence of seasonal differences in nutrient availability Dominguez-Salas et al. Network-based methods describing health, subsystems of physiological processes, and pathological states Mayer et al. The conceptual pipeline from Kaput et al. This pipeline can be operationalized using models of cellular responses, organs, systems, or conditions for designing and testing intervention or clinical studies. The initial tissue-specific framework, describing in molecular detail the processes of transport, metabolism and signaling in steady state, as well as during challenges with altered diet, physical activity, fasting, and sleeping may be developed from model organisms van Ommen et al. However, and importantly for translational human genomics, system thinking and approaches can also be applied directly to humans in clinical settings with the additional concept that determining responses to diet, drugs, treatments, and vaccines based on genetic makeup and molecular phenotyping will be an iterative process Kaput, , Zazzu et al. Perspectives Model systems continue to play an important role for understanding disease and health processes since the types of experiments, control or knowledge of genetic variation, ability to regulate environmental variables, and accessibility to a range of tissues are greater than in human studies. However, the best model for developing an understanding of health and disease is the human. The paradigm shift Kuhn, necessary in translational human health research is the recognition of the necessity to capture the complexity and dynamics of biological processes using omics in response to changing environmental exposures rather than trying to reduce this complexity to artificial levels that may be less meaningful for a real-life situation. This more comprehensive strategy requires extensive molecular phenotyping of humans which includes analysis of environmental, genomic, microbiological and epidemiological factors Kaput and Morine, , Kaput et al. A system approach to human health implies rethinking in vitro and in vivo models with regard to their translatability into human phenotypes: Human clinical study subjects should not only be assessed at homeostasis, e. Such safe challenges can be nutritional, physical, or cognitive in nature van Ommen et al. Classical genomic studies have been technology-driven rather than technology-rooted: This needs to be complemented by more comprehensive systems biology-based investigations deploying a multitude of omic platforms in an integrated fashion. While comprehensive and quantitative omics are rapidly progressing in terms of data generation, quantitative capture and monitoring of the human environment, including diet, lifestyle, and socio-economic status have lagged behind. The bottleneck in knowledge generation has moved from the acquisition to processing, visualization and interpretation of the data. This requires innovative tools and methods including new ways of statistical treatment and biological network analysis. In addition to capturing population-representative profiles, the era of personal gen omics is now emerging. Ultimately, the omics sciences form the analytical basis for an integrated, systematic and quantitative understanding of how a living system functions, be it an organelle, cell, organ, whole organism or even an entire ecosystem. Translational research, and in particular translational genomics research expands pure fundamental science to augment the understanding of the physiological response of an individual to changing environments. This

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knowledge can form the basis to generate new solutions that can be applied in real time to assess, mitigate, improve, or delay disease symptoms and to maintain health. A systems biology approach to nutritional immunology – focus on innate immunity. Clinical and translational medicine in Europe – horizon and beyond. Journal of Translational Medicine. Shanghai, China Angrist M. How smartphones are changing the face of mobile and participatory healthcare: Medical progress and global chronic disease: Personal omics profiling reveals dynamic molecular and medical phenotypes. The personal genome project. G The human genome. Shanghai, China Dankwa-Mullan I. Moving toward paradigm-shifting research in health disparities through translational, transformational, and transdisciplinary approaches. The innovative medicines initiative: The FDA is overcautious on consumer genomics. Engaging basic scientists in translational research: Systems biology and new technologies enable predictive and preventative medicine. Assessment of research models for testing gene-environment interactions. Nutrigenomics research for personalized nutrition and medicine. Discovery-based nutritional systems biology: Consensus statement - understanding health and malnutrition through a systems approach: The Structure of Scientific Revolutions. The extended nutrigenomics – understanding the interplay between the genomes of food, gut microbes, and human host. Worldwide human relationships inferred from genome-wide patterns of variation. Personal genomes in progress: Curating the innate immunity interactome. Systems-based approaches to cardiovascular disease. Rescue of dysfunctional autophagy attenuates hyperinflammatory responses from cystic fibrosis cells. Methylation potential associated with diet, genotype, protein, and metabolite levels in the delta obesity vitamin study. Imperial College Press; Analysis of Biological Systems. Aggregating single patient n-of-1 trials in populations where recruitment and retention was difficult: Cholesterol testing on a smartphone. Vaccinomics, adversomics, and the immune response network theory: The misunderstood limits of folk science: Systems biology approaches for toxicology. Web-enabled and improved software tools and data are needed to measure nutrient intakes and physical activity for personalized health research. The nutrition researcher cohort: A network biology model of micronutrient related health. Challenging homeostasis to define biomarkers for nutrition related health.

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4: Obstetric and Fetal Pharmacology | GLOWM

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This more recent approach and attitude are catalyzed by four trends or developments: Published by Elsevier B. The increasing need for evidenced-based solutions. High-throughput laboratory and clinical data generation. System thinking and analysis. Introduction parallel with these government-funded programs, the U. Translational research has a long history of practice that was Goldman, , and the European Advanced Translational Research formalized by the creation of the U. The goals of investigators conducting basic research. Please cite this article as: FDA has restricted these and other companies from providing associations to trait, phenotype, or disease Green and Farahany, 2. The increasing need for evidenced-based , no restrictions were placed on the right of individuals to own solutions their personal data Angrist, Hence, individuals can and do share their data. Associating indi- and act on related health disparities Dankwa-Mullan et al. However, among the limiting factors for analyzing HapMap International HapMap Consortium, , and related pro- genetic data and outcomes is the lack of reliable and standardized die- jects on human genetic diversity Li et al. High-throughput laboratory and clinical data sures such as body weight, blood pressure and clinical blood chemistry generation parameters, but also by their changing metabolites, transcripts, and proteins. Web-enabled research tools that capture, manage, store, and The second development reinforcing the concept that basic research retrieve these personal molecular phenotype and lifestyle data are un- can be translatable is the ongoing evolution in the ability to quantify available to the research community Stumbo et al. NuGO, the physiologies and genetic makeups of large numbers of study partici- former EU framework six-funded Nutrigenomics Organization and now pants and patients using omics-based and imaging technologies. However, the true strength of micronutrients to millions and soon billions of DNA bases. NRC will come from aggregating individual data with data from other In many cases, omic analysis is done with untargeted methods in a members of the cohort Monteiro et al. NMR-based metabonomics, or MS-based op more in depth understanding of health phenotypes. Targeted tives since at least apps from http: Healthcare Boulos et al. These ment if the diet and lifestyle data captured by apps and devices is of omics sciences have evolved over the last few decades and are prime high quality and accuracy Young et al. Data harmonization examples of how technology has transformed and driven biomedical Lynn et al. Omics comes can usually not be predicted from this knowledge base. Metabo- data obtained from analyzing one person has demonstrated the long- lism and its regulation form a complex interacting set of processes that known facts of biochemical and genetic individuality Williams, This more comprehensive ; Poland et al. Modern system concepts e. A system approach to human health implies rethinking in vitro and relationships of the biological processes. The tion studies should be complemented by crossover, longitudinal human body is not a closed system as demonstrated by changes in studies, in which every subject is its own case and control Kaput blood concentrations of one-carbon metabolites and cofactors as a con- and Morine, Human clinical study subjects should not only be assessed at homeo- Salas et al. Such safe chal- ical processes, and pathological states Mayer et al. The conceptual pipeline from human subjects in clinical studies has often stemmed from recent Kaput et al. This needs to be ciated with health and pathologies and the underlying pathways, complemented by more comprehensive systems biology-based in- functional attributes, and mechanisms. The bottleneck in knowledge generation has moved from the acqui- This pipeline can be operationalized using models of cellular re- sition to processing, visualization and interpretation of the data. This sponses, organs, systems, or conditions for designing and testing inter- requires innovative tools and methods including new ways of statis- vention or clinical studies. Ultimately, the omics sciences model organisms van Ommen et al. However, and importantly form the analytical basis for an integrated, systematic and quantitative for translational human genomics, system thinking and approaches can understanding of how a living system functions, be it an

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organelle, also be applied directly to humans in clinical settings with the additional cell, organ, whole organism or even an entire ecosystem. Translational research, and in particular translational genomics research expands pure funda- 6. Perspectives mental science to augment the understanding of the physiological response of an individual to changing environments. This knowledge Model systems continue to play an important role for understanding can form the basis to generate new solutions that can be applied in disease and health processes since the types of experiments, control or real time to assess, mitigate, improve, or delay disease symptoms and knowledge of genetic variation, ability to regulate environmental vari- to maintain health. The paradigm shift Kuhn, nec- essary in translational human health research is the recognition of the The authors are employed by the Nestle Institute of Health Sciences. A systems biology approach to nutritional Translational genomics should therefore investigate how genomic immunology â€” focus on innate immunity. Personal genomes in progress: PLoS One 9, 9â€” How smartphones are changing G. Systems-based approaches to cardiovascular Callahan, D. Medical progress and global chronic disease: Analysis of Biological Systems. The personal genome project. Aggregating single patient n-of-1 trials in populations where doi. Cholesterol testing on a smartphone. Science 80 , Chip 14, â€” Proceedings of the Sino- Oberg, A. Moving toward paradigm-shifting research in health disparities through trans- Clin. Public Health , Rozenblit, L. The misunderstood limits of folk science: DNA meth- Slikker Jr. Systems biology ylation potential: Web-enabled and improved software tools and The nutrition researcher cohort: The innovative medicines initiative: The FDA is overcautious on consumer genomics. A network biology model of micronutrient related health. Engaging basic scientists in translational research: Systems biology and new technologies en- Mathers, J. Challenges of molecular nutrition research 6: Assessment of research models for testing gene-environment interac- The International HapMap Project. Nutrigenomics research for personalized nutrition and medicine. Discovery-based nutritional systems biology: Consensus statement - understanding health and malnu- Shue, B. The extended nutrigenomics â€” understanding the L. Worldwide human re- Vech, C. Science 80 , Deen, E. Incorporating guidelines for use of S. IT future of medicine: Science 80 , â€” Targeting the human genome-microbiome axis for drug discovery: The Basis for the Genetotropic Concept.

5: NeuroToxicology Editorial Board

1 Mirkes Role of Apoptosis in Normal and Abnormal Development 2 Abbott Signal transduction pathways as targets for teratogens 3 Hansen Nutrition in Developmental Toxicology 4 Ellis-Hutchings & Rogers Epigenetic Mechanisms- Role of DNA Methylation, Histone Modifications & Imprinting 5 Kaput, Chen, Slikker, Jr. Personalized Nutrition and Medicine in Perinatal Development 6 Hunter & Hartig.

6: Translational genomics

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7: Table of contents for Developmental toxicolog

NCTR Director, William Slikker, Jr., Ph.D., was a featured speaker at the IARS and the Safety of Key Inhaled and Intravenous Drugs in Pediatrics (SAFEKIDS) International Science Symposium held.

8: - NLM Catalog Result

personalized nutrition and medicine: impact on perinatal development symposium-urban (17th floor) Chairpersons:

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William Slikker, Jr., National Center for Toxicological Research, U.S. Food and Drug Administration and.

9: ATG KUSSMANN KAPUT Translational Genomics | Martin Kussmann - www.enganchecubano.com

The development of nutrigenomics and nutrigenetics as well as the fledgling efforts of using systems level analyses in nutrition auger well for the future development of personalized nutrition. For example Subbiah [67] recently discussed the development of nutraceuticals to prevent and mange thrombosis in women carrying thrombophilic gene.

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