

Chapter 1 : Erowid Drug Testing Vaults : Misc Info

Highlights Type II is the main mechanism of phage photoinactivation by Tri-Py +-Me-PF and Tetra-Py +-Me. The afforded degree of protection varied with the concentration of the scavengers. The scavenging effect on PDI was higher in T4-like (DNA) than in Q β (RNA) phages. The type of phage must be considered when the mechanisms involved in PDI is studied.

All registrations must be completed prior to the application being submitted. Registration can take 6 weeks or more, so applicants should begin the registration process as soon as possible. The NIH Policy on Late Submission of Grant Applications states that failure to complete registrations in advance of a due date is not a valid reason for a late submission. The same DUNS number must be used for all registrations, as well as on the grant application. The renewal process may require as much time as the initial registration. Obtaining an eRA Commons account can take up to 2 weeks. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH support. Additional Information on Eligibility Number of Applications Applicant organizations may submit more than one application, provided that each application is scientifically distinct. The NIH will not accept duplicate or highly overlapping applications under review at the same time. This means that the NIH will not accept: A new A0 application that is submitted before issuance of the summary statement from the review of an overlapping new A0 or resubmission A1 application. A resubmission A1 application that is submitted before issuance of the summary statement from the review of the previous new A0 application. An application that has substantial overlap with another application pending appeal of initial peer review see NOT-OD Application and Submission Information 1. See your administrative office for instructions if you plan to use an institutional system-to-system solution. Conformance to the requirements in the Application Guide is required and strictly enforced. Applications that are out of compliance with these instructions may be delayed or not accepted for review. Letter of Intent Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows IC staff to estimate the potential review workload and plan the review. By the date listed in Part 1. Overview Information , prospective applicants are asked to submit a letter of intent that includes the following information: Describe the central scientific theme of the proposed research program. Describe the potential gain in fundamental knowledge of immune interactions and functions at the maternal-fetal interface. Describe the novelty or innovation of the research in terms of how the outcome will lead to new and potentially transformative discoveries in the role and mechanisms of immune cells during pregnancy. For descriptive studies, describe how the descriptive studies lay a foundation that may lead to the discovery of novel phenomena or major advances in the future. Demonstrate how the descriptive studies suggest and explore creative, original, or potentially transformative concepts in understanding immune interactions, function, and mechanisms at the maternal-fetal interface. Provide a plan for management and quality control of data for the proposed study, including the statistical design including power calculations and analysis plan for the animal studies. Demonstrate the feasibility of the proposed approach. For applications proposing the use of animal models, include a justification for the use of the proposed animal model with respect to their relevance to human pregnancy. Provide any institutional letters of support, memoranda of understanding MOU and letters of collaboration specific to the proposed research. For projects obtaining samples from independently funded clinical trials, include an MOU from the clinical trial director agreeing to provide samples according to a timeline established by the applicant. The MOU for the use of biological human samples should confirm agreement among the various parties that outlines their expectations of the agreement in the following areas: All applications, regardless of the amount of direct costs requested for any one year, should address a Data Sharing Plan. Therefore, the Resource Sharing plan should include a summary of how the applicant will manage data submission and interactions with the chosen portal s. Only limited Appendix materials are allowed. As an attachment, for completed or draft consent forms for the use of biological human samples from ongoing or completed clinical research, attach "Informed Consent to Use Samples. Within the forms, the following items should be addressed: Any

incentives provided to subjects to participate in the proposed study, if in addition to those under the parent clinical research, should be clearly described and justified; 5 indication that the samples can be used for third party analyses and proposed immune studies. Section 3 - Protection and Monitoring Plans 3. Foreign Institutions Foreign non-U. Submission Dates and Times Part I. Overview Information contains information about Key Dates and times. Applicants are encouraged to submit applications before the due date to ensure they have time to make any application corrections that might be necessary for successful submission. When a submission date falls on a weekend or Federal holiday , the application deadline is automatically extended to the next business day. Organizations must submit applications to Grants. Applicants are responsible for viewing their application before the due date in the eRA Commons to ensure accurate and successful submission. Paper applications will not be accepted. Applicants must complete all required registrations before the application due date. Eligibility Information contains information about registration. For assistance with your electronic application or for more information on the electronic submission process, visit Applying Electronically. If you encounter a system issue beyond your control that threatens your ability to complete the submission process on-time, you must follow the Guidelines for Applicants Experiencing System Issues. See more tips for avoiding common errors. Upon receipt, applications will be evaluated for completeness and compliance with application instructions by the Center for Scientific Review and responsiveness by components of participating organizations , NIH. Post Submission Materials Applicants are required to follow the instructions for post-submission materials, as described in the policy. Any instructions provided here are in addition to the instructions in the policy. Application Review Information 1. Criteria Only the review criteria described below will be considered in the review process. As part of the NIH mission , all applications submitted to the NIH in support of biomedical and behavioral research are evaluated for scientific and technical merit through the NIH peer review system. In addition, for applications involving clinical trials: A proposed Clinical Trial application may include study design, methods, and intervention that are not by themselves innovative but address important questions or unmet needs. Additionally, the results of the clinical trial may indicate that further clinical development of the intervention is unwarranted or lead to new avenues of scientific investigation. Overall Impact Reviewers will provide an overall impact score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field s involved, in consideration of the following review criteria and additional review criteria as applicable for the project proposed. Scored Review Criteria Reviewers will consider each of the review criteria below in the determination of scientific merit, and give a separate score for each. An application does not need to be strong in all categories to be judged likely to have major scientific impact. For example, a project that by its nature is not innovative may be essential to advance a field. Significance Does the project address an important problem or a critical barrier to progress in the field? Is there a strong scientific premise for the project? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field? Specific to this FOA: Do the studies lay a foundation that may lead to the discovery of novel phenomena or major advances in the future? For trials focusing on clinical or public health endpoints, is this clinical trial necessary for testing the safety, efficacy or effectiveness of an intervention that could lead to a change in clinical practice, community behaviors or health care policy? For trials focusing on mechanistic, behavioral, physiological, biochemical, or other biomedical endpoints, is this trial needed to advance scientific understanding? If Early Stage Investigators or those in the early stages of independent careers, do they have appropriate experience and training? If established, have they demonstrated an ongoing record of accomplishments that have advanced their field s? Do they have appropriate expertise in study coordination, data management and statistics? For a multicenter trial, is the organizational structure appropriate and does the application identify a core of potential center investigators and staffing for a coordinating center? Innovation Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed? Approach Are the overall

strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Have the investigators presented strategies to ensure a robust and unbiased approach, as appropriate for the work proposed? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed? Have the investigators presented adequate plans to address relevant biological variables, such as sex, for studies in vertebrate animals or human subjects? Do the proposed studies utilize novel and potentially transformative concepts for the understanding of immune interactions, functions, and mechanisms at the maternal-fetal interface? If applicable, do the consent forms provide sufficient detail to clarify the process of subject participation? Is the trial appropriately designed to conduct the research efficiently? Are potential ethical issues adequately addressed? Is the process for obtaining informed consent or assent appropriate? Is the eligible population available? Are the plans for recruitment outreach, enrollment, retention, handling dropouts, missed visits, and losses to follow-up appropriate to ensure robust data collection? Are the planned recruitment timelines feasible and is the plan to monitor accrual adequate? Are the plans to standardize, assure quality of, and monitor adherence to, the trial protocol and data collection or distribution guidelines appropriate? Is there a plan to obtain required study agent s? Does the application propose to use existing available resources, as applicable? Data Management and Statistical Analysis Are planned analyses and statistical approach appropriate for the proposed study design and methods used to assign participants and deliver interventions? Are the procedures for data management and quality control of data adequate at clinical site s or at center laboratories, as applicable? Have the methods for standardization of procedures for data management to assess the effect of the intervention and quality control been addressed? Is there a plan to complete data analysis within the proposed period of the award? Environment Will the scientific environment in which the work will be done contribute to the probability of success?

Chapter 2 : Organic Reactions

While ANG II-dependent signaling is the focus of this review, significant advancement has also been made for signaling mechanisms utilized by new members of the angio-

Cellular level[edit] At the cellular level, much of the variance in insulin sensitivity between untrained, non-diabetic humans may be explained by two mechanisms: In the long term, diet has the potential to change the ratio of polyunsaturated to saturated phospholipids in cell membranes, correspondingly changing cell membrane fluidity; full impact of such changes is not fully understood, but it is known that the percentage of polyunsaturated phospholipids is strongly inversely correlated with insulin resistance. Cortisol counteracts insulin, contributes to hyperglycemia-causing hepatic gluconeogenesis, [52] and inhibits the peripheral utilization of glucose, which eventually leads to insulin resistance. Mice without JNK1 -signaling do not develop insulin resistance under dietary conditions that normally produce it. As short-term overdosing of insulin causes short-term insulin resistance, it has been hypothesized that chronic high dosing contributes to more permanent insulin resistance. This link seems to exist under diverse causes of insulin resistance. It also is based on the finding that insulin resistance may be reversed rapidly by exposing cells to mitochondrial uncouplers, electron transport chain inhibitors, or mitochondrial superoxide dismutase mimetics. It has long been observed that patients who have had some kinds of bariatric surgery have increased insulin sensitivity and even remission of type 2 diabetes. This suggested similar surgery in humans, and early reports in prominent medical journals [60] are that the same effect is seen in humans, at least the small number who have participated in the experimental surgical program. The speculation is, that some substance is produced in the mucosa of that initial portion of the small intestine that signals body cells to become insulin resistant. If the producing tissue is removed, the signal ceases and body cells revert to normal insulin sensitivity. No such substance has been found as yet, and the existence of such a substance remains speculative. The resulting increase in blood glucose may raise levels outside the normal range and cause adverse health effects, depending on dietary conditions. When these cells fail to respond adequately to circulating insulin, blood glucose levels rise. The liver helps regulate glucose levels by reducing its secretion of glucose in the presence of insulin. Insulin resistance normally refers to reduced glucose-lowering effects of insulin. However, other functions of insulin can also be affected. For example, insulin resistance in fat cells reduces the normal effects of insulin on lipids and results in reduced uptake of circulating lipids and increased hydrolysis of stored triglycerides. Increased mobilization of stored lipids in these cells elevates free fatty acids in the blood plasma. Elevated blood fatty-acid concentrations associated with insulin resistance and diabetes mellitus Type 2, reduced muscle glucose uptake, and increased liver glucose production all contribute to elevated blood glucose levels. High plasma levels of insulin and glucose due to insulin resistance are a major component of the metabolic syndrome. If insulin resistance exists, more insulin needs to be secreted by the pancreas. If this compensatory increase does not occur, blood glucose concentrations increase and type 2 diabetes or latent autoimmune diabetes of adults occurs. The insulin, in turn, makes insulin-sensitive tissues in the body primarily skeletal muscle cells, adipose tissue, and liver absorb glucose, and thereby lower the blood glucose level. In an insulin-resistant person, normal levels of insulin do not have the same effect in controlling blood glucose levels. During the compensated phase on insulin resistance, insulin levels are higher, and blood glucose levels are still maintained. If compensatory insulin secretion fails, then either fasting impaired fasting glucose or postprandial impaired glucose tolerance glucose concentrations increase. Eventually, type 2 diabetes or latent autoimmune diabetes occurs when glucose levels become higher throughout the day as the resistance increases and compensatory insulin secretion fails. The elevated insulin levels also have additional effects see insulin that cause further abnormal biological effects throughout the body. Insulin resistance often progresses to full Type 2 diabetes mellitus T2DM or latent autoimmune diabetes of adults. Recent research is investigating the roles of adipokines the cytokines produced by adipose tissue in insulin resistance. Certain drugs also may be associated with insulin resistance e. Exercise reverses this process in muscle tissue, [70] but if it is left unchecked, it may contribute to insulin resistance. Elevated blood levels of glucoseâ€”regardless of

cause lead to increased glycation of proteins with changes, only a few of which are understood in any detail, in protein function throughout the body. With respect to visceral adiposity, a great deal of evidence suggests two strong links with insulin resistance. In numerous experimental models, these proinflammatory cytokines disrupt normal insulin action in fat and muscle cells, and may be a major factor in causing the whole-body insulin resistance observed in patients with visceral adiposity. Second, visceral adiposity is related to an accumulation of fat in the liver, a condition known as non-alcoholic fatty liver disease NAFLD. The result of NAFLD is an excessive release of free fatty acids into the bloodstream due to increased lipolysis, and an increase in hepatic glycogenolysis and hepatic glucose production, both of which have the effect of exacerbating peripheral insulin resistance and increasing the likelihood of Type 2 diabetes mellitus. The same levels apply three hours after the last meal. Then blood glucose levels are measured over the following two hours. Interpretation is based on WHO guidelines. After two hours a glycemia less than 7. An oral glucose tolerance test OGTT may be normal or mildly abnormal in simple insulin resistance. Often, there are raised glucose levels in the early measurements, reflecting the loss of a postprandial peak after the meal in insulin production. Extension of the testing for several more hours may reveal a hypoglycemic "dip," that is a result of an overshoot in insulin production after the failure of the physiologic postprandial insulin response. The test is rarely performed in clinical care, but is used in medical research, for example, to assess the effects of different medications. The rate of glucose infusion commonly is referred to in diabetes literature as the GINF value. Through a peripheral vein, insulin is infused at 10 mU per m² per minute. The rate of glucose infusion is determined by checking the blood sugar levels every five to ten minutes. If high levels 7. Very low levels 4. Glucose may be labeled with either stable or radioactive atoms. Commonly used tracers are H glucose radioactive, 6,6 ²H-glucose stable and C Glucose stable. Prior to beginning the hyperinsulinemic period, a 3h tracer infusion enables one to determine the basal rate of glucose production. During the clamp, the plasma tracer concentrations enable the calculation of whole-body insulin-stimulated glucose metabolism, as well as the production of glucose by the body. The test correlates well with the euglycemic clamp, with less operator-dependent error. This test has been used to advance the large body of research relating to the metabolic syndrome. Blood glucose is checked at zero, 30, 60, 90, and minutes, and thereafter, every 10 minutes for the last half-hour of the test. These last four values are averaged to determine the steady-state plasma glucose level SSPG. Both employ fasting insulin and glucose levels to calculate insulin resistance, and both correlate reasonably with the results of clamping studies. Research shows that a low-carbohydrate diet may help. By contrast, growth hormone replacement therapy may be associated with increased insulin resistance. Insulin resistance is often associated with abnormalities in lipids particularly high blood triglycerides and low high density lipoprotein.

Chapter 3 : Insulin resistance - Wikipedia

Clay will be taken as $\hat{A} \hat{A} \frac{1}{2} 20 \text{ kN/m}^3$, so taking $\hat{A}^a w \hat{A} \frac{1}{2} 10 \text{ kN/m}^3$ and $f u \hat{A} \frac{1}{2} 0.6$ for example, a typical range of values for K s may be calculated from Equation

This can be explained by assuming that the products of the bond-breaking reaction become more stable as the number of alkyl groups increases. The activation energy for the chain-propagation steps in free-radical bromination reactions is significantly larger than the activation energy for these steps during chlorination. As a result, free-radical bromination reactions are more selective than chlorination reactions. Bromination reactions are far more likely to give the product predicted from the relative stability of the free-radical intermediate. Bromination of 2-methylpropane, for example, gives almost exclusively 2-bromomethylpropane, not the statistically more likely 1-bromomethylpropane.

Bimolecular Nucleophilic Substitution or SN2 Reactions

Most of our knowledge of the mechanisms of chemical reactions has come from the study of the factors that influence the rate of these reactions. The type of reaction that has been studied more than any other involves attack by a nucleophile on a saturated carbon atom. Consider the following reaction, for example, which converts an alkyl bromide into an alcohol. In the course of this reaction, one nucleophile the OH⁻ ion is substituted for another the Br⁻ ion. This is therefore a nucleophilic substitution reaction. It attacks the carbon atom at a point directly opposite to the Br substituent or leaving group. When this happens, a pair of nonbonding electrons on the OH⁻ ion are used to form a covalent bond to the carbon atom at the same time that the carbon-bromine is broken, as shown in the figure below. Because the rate-limiting step in this reaction involves both the CH₃Br and OH⁻ molecules, it is called a bimolecular nucleophilic substitution, or SN₂, reaction. The most important point to remember about the mechanism of SN₂ reactions is that they occur in a single step. The species in the middle of Figure O3. If you envision this reaction as an endless series of snapshots that capture the infinitesimally small changes which occur as one bond forms and the other bond breaks, the transition state is the snapshot in this series that has the highest energy and is therefore the least stable. The transition state has an infinitesimally short lifetime, on the order of seconds. In the course of an SN₂ reaction, the other three substituents on the carbon atom are "flipped" from one side of the atom to the other. This inevitably leads to inversion of the configuration at a stereocenter. Consider the following reaction, for example, in which cisbromomethylcyclopentane is converted into transmethylcyclopentanol. Or the reaction in which the 2-butanol. Consider the reaction between the OH⁻ ion and t-butyl bromide, for example. The rate of this reaction depends only on the concentration of the alkyl bromide. Adding more OH⁻ ion to the solution has no effect on the rate of reaction. As one might expect, the pair of electrons in the C Br bond end up on the more electronegative bromine atom. Because the bromine atom has formally gained an electron from the carbon atom, it is now a negatively charged Br⁻ ion. Because the carbon atom has formally lost an electron, it is now a "carbocation. If this reaction is done in water, the next step is extremely fast. Water, on the other hand, is a reasonably good Lewis base. A Lewis acid-base reaction therefore rapidly occurs in which a pair of nonbonding electrons on a water molecule are donated to the carbocation to form a covalent C O bond. The product of this reaction is a stronger acid than water. As a result, it transfers a proton to water. Because the slowest step of this reaction only involves t-butyl bromide, the overall rate of reaction only depends on the concentration of this species. This is therefore a unimolecular nucleophilic substitution, or SN₁, reaction. The central carbon atom in the t-butyl carbocation formed in the first step of this reaction is planar, as shown in the figure below. This means that water can attack this carbocation in the second step with equal probability from either side of the carbon atom. This has no effect on the products of this reaction, because the starting material is not optically active. But what would happen if we started with an optically active halide, such as 2-bromobutane? Regardless of whether we start with the R or S isomer, we get the same intermediate when the C Br bond breaks. The intermediate formed in the first step in the SN₁ mechanism is therefore achiral. This term traces back to the Latin racemus, which means "a cluster of grapes. SN₁ reactions are therefore said to proceed with racemization. If we start with a pure sample of R bromobutane, for example, we expect the product of the SN₁ reaction with the OH⁻ ion to be a racemic mixture of the two enantiomers of

2-butanol. We are now ready to address a pair of important questions. The SN1 reaction proceeds through a carbocation intermediate, and the stability of these ions decreases in the following order. Organic chemists explain this by noting that alkyl groups are slightly "electron releasing. This tends to delocalize the charge over a larger volume of the molecule, which stabilizes the carbocation. In this case, the difference is much larger. In theory, both starting materials could undergo both reaction mechanisms. Elimination Reactions Why do we need to worry about whether a nucleophilic substitution reaction occurs by an SN1 or SN2 mechanism? At first glance, it would appear that the same product is obtained regardless of the mechanism of the reaction. Consider the following substitution reaction, for example. The only apparent difference between the two mechanisms is the stereochemistry of the product. If the reaction proceeds through an SN2 mechanism, it gives inversion of configuration conversion of an R starting material into an S product, or vice versa. If the reaction proceeds through a carbocation intermediate via an SN1 mechanism, we get a racemic mixture. The importance of understanding the mechanism of nucleophilic substitution reactions can best be appreciated by studying the distribution of products of the example given above. When 2-bromopropane is allowed to react with the methoxide ion in methanol, less than half of the starting material is converted into methyl isopropyl ether; the rest is transformed into 2-propene. It is therefore an example of an elimination reaction. Starting materials that are likely to undergo a bimolecular SN2 reaction undergo elimination reactions by a bimolecular E2 mechanism. This is a one-step reaction in which the nucleophile attacks a C H bond on the carbon atom adjacent to the site of SN2 reaction. Starting materials that are likely to undergo a unimolecular SN1 reaction undergo elimination reactions by a unimolecular E1 mechanism. As might be expected, the rate-limiting step is the formation of the carbocation. The electrons in the C H bond that is broken are donated to the empty orbital on the carbocation to form a double bond. Substitution Versus Elimination Reactions There are three ways of pushing the reaction between an alkyl halide and a nucleophile toward elimination instead of substitution. Start with a highly substituted substrate, which is more likely to undergo elimination. The vast majority of the starting material goes on to form the product expected for an SN2 reaction. More than half of a secondary alkyl bromide undergoes elimination under the same conditions, as we have already seen. Use a very strong base as the nucleophile. In the presence of the ethoxide ion, which is a much stronger base, the product of the reaction is predominantly the alkene. Increase the temperature at which the reaction is run. Because both E1 and E2 reactions lead to an increase in the number of particles in the system, they are associated with a positive entropy term. Thus, increasing the temperature of the reaction makes the overall free energy of reaction more negative, and the reaction more favorable. Methyl halides and primary alkyl halides such as CH₃CH₂Br Secondary alkyl halides undergo SN2 reactions when handled gently at low temperatures and with moderate strength nucleophiles. At high temperatures, or in the presence of a strong base, secondary halides undergo E2 elimination reactions. Tertiary halides undergo a combination of SN1 and E1 reactions. If the reaction is kept cool, and the nucleophile is a relatively weak base, it is possible to get nucleophilic substitution. At high temperatures, or with strong bases, elimination reactions predominate.

Chapter 4 : Ejection seat - Wikipedia

3. Alcohols *oa.* 3 alcohol- acid catalyzed dehydration: *b.* 2o, 3o alcohol dehydration with POCl_3 3: *c.* 3o alcohol to alkyl halide using HX ($\text{X} = \text{Cl}, \text{Br}, \text{I}$): *d.* 1o, 2o alcohol to alkyl halide using SOCl_2 .

A bungee -assisted escape from an aircraft took place in In Everard Calthrop , an early inventor of parachutes , patented an ejector seat using compressed air. Dragomir patented his "catapult-able cockpit" at the French Patent Office. Prior to this, the only means of escape from an incapacitated aircraft was to jump clear "bail out" , and in many cases this was difficult due to injury, the difficulty of egress from a confined space, g forces , the airflow past the aircraft, and other factors. Early models were powered by compressed air and the first aircraft to be fitted with such a system was the Heinkel He prototype jet-engined fighter in One of the He test pilots, Helmut Schenk, became the first person to escape from a stricken aircraft with an ejection seat on 13 January after his control surfaces iced up and became inoperative. The fighter, being used in tests of the Argus As impulse jets for Fieseler Fi missile development, had its usual HeS 8A turbojets removed, and was towed aloft from the Erprobungsstelle Rechlin central test facility of the Luftwaffe in Germany by a pair of Bf C tugs in a heavy snow-shower. To save pilots a spring-driven catapult seat was developed in a few months time, but the prototype has been destroyed in during an air raid, shortly before its maiden flight. No one other prototype was finished before the fall of Budapest. A gunpowder ejection seat was developed by Bofors and tested in for the Saab The first test in the air was on a Saab 17 on 27 February , [4] and the first real use occurred by Lt. Bengt Johansson [note 2] on 29 July after a mid-air collision between a J 21 and a J In this system, the seat rode on wheels set between two pipes running up the back of the cockpit. When lowered into position, caps at the top of the seat fitted over the pipes to close them. Cartridges, basically identical to shotgun shells, were placed in the bottom of the pipes, facing upward. When fired, the gases would fill the pipes, "popping" the caps off the end, and thereby forcing the seat to ride up the pipes on its wheels and out of the aircraft. By the end of the war, the Dornier Do Pfeil " primarily from it having a rear-mounted engine of the twin engines powering the design powering a pusher propeller located at the aft end of the fuselage presenting a hazard to a normal "bailout" escape " and a few late-war prototype aircraft were also fitted with ejection seats. After World War II, the need for such systems became pressing, as aircraft speeds were getting ever higher, and it was not long before the sound barrier was broken. Manual escape at such speeds would be impossible. The United States Army Air Forces experimented with downward-ejecting systems operated by a spring , but it was the work of James Martin and his company Martin-Baker that proved crucial. Shortly afterward, on 17 August , 1st Sgt. Larry Lambert was the first live U. Lynch demonstrated the ejection seat at the Daily Express Air Pageant in , ejecting from a Meteor. Early seats used a solid propellant charge to eject the pilot and seat by igniting the charge inside a telescoping tube attached to the seat. As aircraft speeds increased still further, this method proved inadequate to get the pilot sufficiently clear of the airframe. In , the Convair F Delta Dagger was the first aircraft to be fitted with a rocket-propelled seat. Martin-Baker developed a similar design, using multiple rocket units feeding a single nozzle. The greater thrust from this configuration had the advantage of being able to eject the pilot to a safe height even if the aircraft was on or very near the ground. In the early s, deployment of rocket-powered ejection seats designed for use at supersonic speeds began in such planes as the Convair F Delta Dart. Following an accident on 30 July in the attempted launch of a D drone , two Lockheed M [7] crew members ejected at Mach 3. The pilot was recovered successfully, but the launch control officer drowned after a water landing. Despite these records, most ejections occur at fairly low speeds and altitudes, when the pilot can see that there is no hope of regaining aircraft control before impact with the ground. Late in the Vietnam War, the U. Air Force and U. Navy became concerned about its pilots ejecting over hostile territory and those pilots either being captured or killed and the losses in men and aircraft in attempts to rescue them. Three companies submitted papers for further development: A Rogallo wing design by Bell Systems; a gyrocopter design by Kaman Aircraft ; and a mini-conventional fixed wing aircraft employing a Princeton Wing i. All three, after ejection, would be propelled by small turbojet engine developed for target drones. With the exception of the Kaman design, the pilot would still be required to parachute to the ground after reaching a

safety-point for rescue. It came close to being tested with a special landing-gear platform attached to the AERCAB ejection seat for first-stage ground take offs and landings with a test pilot. The pilot was recovered by helicopter. The pilot typically experiences an acceleration of about 12–14 g. Compression fractures of vertebrae are a recurrent side effect of ejection. It was theorised early on that ejection at supersonic speeds would be unsurvivable; extensive tests, including Project Whoosh with chimpanzee test subjects, were undertaken to determine that it was feasible. Documented evidence exists that pilots of the US [14] and Indian navies have performed this feat. Early models of the ejection seat were equipped with only an overhead ejection handle which doubled in function by forcing the pilot to assume the right posture and by having him pull a screen down to protect both his face and oxygen mask from the subsequent air blast. Please help improve this article by adding citations to reliable sources. Unsourced material may be challenged and removed. May Learn how and when to remove this template message A warning applied on the cockpit side of some aircraft using an ejection seat system intended especially for the maintenance and emergency crews The "standard" ejection system operates in two stages. First, the entire canopy or hatch above the aviator is opened, shattered, or jettisoned, and the seat and occupant are launched through the opening. In most earlier aircraft this required two separate actions by the aviator, while later egress system designs, such as the Advanced Concept Ejection Seat model 2 ACES II, perform both functions as a single action. Stricklin was not injured. The A uses connected firing handles that activate both the canopy jettison systems, followed by the seat ejection. The F has the same connected system as the A seat. Both handles accomplish the same task, so pulling either one suffices. Early models of the F Starfighter were equipped with a Downward Track ejection seat due to the hazard of the T-tail. In order to make this work, the pilot was equipped with "spurs" which were attached to cables that would pull the legs inward so the pilot could be ejected. Following this development, some other egress systems began using leg retractors as a way to prevent injuries to flailing legs, and to provide a more stable center of gravity. Some models of the F were equipped with upward-ejecting seats. Similarly, two of the six ejection seats on the B Stratofortress fire downward, through hatch openings on the bottom of the aircraft; the downward hatches are released from the aircraft by a thruster that unlocks the hatch, while gravity and wind remove the hatch and arm the seat. The four seats on the forward upper deck two of them, EWO and Gunner, facing the rear of the airplane fire upwards as usual. Any such downward-firing system is of no use on or near the ground if aircraft is in level flight at the time of the ejection. Aircraft designed for low-level use sometimes have ejection seats which fire through the canopy, as waiting for the canopy to be ejected is too slow. Many aircraft types e. The MDC is initiated when the eject handle is pulled, and shatters the canopy over the seat a few milliseconds before the seat is launched. This system was developed for the Hawker Siddeley Harrier family of VTOL aircraft as ejection may be necessary while the aircraft was in the hover, and jettisoning the canopy might result in the pilot and seat striking it. The A Thunderbolt II is equipped with canopy breakers on either side of its headrest in the event that the canopy fails to jettison. The T-6 is also equipped with such breakers if the MDC fails to detonate. In ground emergencies, a ground crewman or pilot can use a breaker knife attached to the inside of the canopy to shatter the transparency. The A-6 Intruder and EA-6B Prowler seats were capable of ejecting through the canopy, with canopy jettison a separate option if there is enough time. CD and TCP systems cannot be used with canopies made of flexible materials, such as the Lexan polycarbonate canopy used on the F Soviet VTOL naval fighter planes such as the Yakovlev Yak were equipped with ejection seats which were automatically activated during at least some part of the flight envelope. Halfway between simply "bailing out" and using explosive-eject systems, Drag Extraction uses the airflow past the aircraft or spacecraft to move the aviator out of the cockpit and away from the stricken craft on a guide rail. Some operate like a standard ejector seat, by jettisoning the canopy, then deploying a drag chute into the airflow. That chute pulls the occupant out of the aircraft, either with the seat or following release of the seat straps, who then rides off the end of a rail extending far enough out to help clear the structure. In the case of the Space Shuttle, the astronauts would have ridden a long, curved rail, blown by the wind against their bodies, then deployed their chutes after free-falling to a safe altitude. Crewmember escape capsule from a B Hustler Encapsulated Seat egress systems were developed for use in the B Hustler and B Valkyrie supersonic bombers. These seats were enclosed in an

air-operated clamshell, which permitted the aircrew to escape at airspeeds and altitudes high enough to otherwise cause bodily harm. These seats were designed to allow the pilot to control the plane even with the clamshell closed, and the capsule would float in case of water landings. Some aircraft designs, such as the General Dynamics F-16, do not have individual ejection seats, but instead, the entire section of the airframe containing the crew can be ejected as a single capsule. In this system, very powerful rockets are used, and multiple large parachutes are used to bring the capsule down, in a manner similar to the Launch Escape System of the Apollo spacecraft. On landing, an airbag system is used to cushion the landing, and this also acts as a flotation device if the Crew Capsule lands in water. Zero-zero ejection seat[edit] K DM Ejection seat used on MiG A zero-zero ejection seat is designed to safely extract upward and land its occupant from a grounded stationary position i. Parachutes require a minimum altitude for opening, to give time for deceleration to a safe landing speed. Thus, prior to the introduction of zero-zero capability, ejections could only be performed above minimum altitudes and airspeeds. If the seat was to work from zero aircraft altitude, the seat would have to lift itself to a sufficient altitude. These early seats fired the seat from the aircraft with a cannon, providing the high impulse needed over the very short length on the cannon barrel within the seat. This limited the total energy, and thus the additional height possible, as otherwise the high forces needed would crush the pilot. Zero-zero technology uses small rockets to propel the seat upward to an adequate altitude and a small explosive charge to open the parachute canopy quickly for a successful parachute descent, so that proper deployment of the parachute no longer relies on airspeed and altitude. The seat cannon clears the seat from the aircraft, then the under-seat rocket pack fires to lift the seat to altitude. As the rockets fire for longer than the cannon, they do not require the same high forces. Zero-zero rocket seats also reduced forces on the pilot during any ejection, reducing injuries and spinal compression. Other aircraft[edit] The Kamov Ka-26, which entered limited service with Russian forces in 1975, was the first production helicopter with an ejection seat. The system is similar to that of a conventional fixed-wing aircraft however the main rotors are equipped with explosive bolts to jettison the blades moments before the seat is fired. The Soviet shuttle "Buran" was planned to be fitted with KRB KMF35 seats, but it was unmanned on its single flight; the seats were never installed. The only commercial jetliner ever fitted with ejection seats was the Soviet Tupolev Tu-142. However, the seats were present in the prototype only, and were only available for the crew and not the passengers. The Tu-142 that crashed at the Paris Air Show in 1985 was a production model, and did not have ejection seats. The only spacecraft ever flown with installed ejection seats were the Space Shuttle, the Soviet Vostok and American Gemini series.

Chapter 5 : Table of Contents

Applications are sought that (1) identify and define immune mechanisms during normal pregnancy, and/or (2) identify and elucidate mechanisms of immune responses triggered by infections vaccinations, and/or ionizing radiation during pregnancy.

Chapter 6 : RFA-AI Immune Mechanisms at the Maternal-Fetal Interface (R01 Clinical Trial Optional)

*Quality Control of Photosystem II: The Mechanisms for Avoidance and Tolerance of Light and Heat Stresses are Closely Linked to Membrane Fluidity of the Thylakoids Yasusi Yamamoto * Graduate School of Natural Science and Technology, Okayama University, Okayama, Japan.*