DOWNLOAD PDF INVESTIGATION: AN INTRODUCTION TO DX E/T53

Chapter 1 : Law Enforcement & Policing

Abstract O-GlcNAcylation is a dynamic protein modification which has been studied mainly in metazoans. However, defects in infection of A. O-GlcNAcylation, Plum pox virus, Potyvirus, Capsid protein, Mass spectrometry Introduction In the sophisticated network of mechanisms that regulates gene expression and gene product function, a major role is played by a large number of post-translational modifications. Among them, glycosylation is one of the most varied, complex and widespread Spiro, At least 41 different sugarâ€"amino acid linkages are known. These glycopeptide bonds have been arranged in five distinct groups Spiro, Whereas the most usual protein glycosylations add complex oligosaccharides to asparagine residues in the endoplasmic reticulum and the Golgi apparatus, O-GlcNAcylation is much simpler, involving modification of serine or threonine residues of nuclear and cytoplasmic proteins with a D-N-acetylglucosamine monosaccharide Hart et al. Although O-GlcNAcylation went unnoticed until the early s, it has been revealed as an abundant post-translational modification that is involved in a broad array of cellular processes in of most organisms Butkinaree et al. O-GlcNAcylation is a dynamic process that is often linked to phosphorylation. O-GlcNAcylation is involved in sensing environmental signals and nutrient status to regulate signaling cascades. Defects in O-GlcNAcylation underlie several important diseases, especially diabetes and neurodegenerative disorders Butkinaree et al. In Caenorhabditis elegans, while deletion of the unique OGT causes severe defect in metabolism, it is not lethal Hanover et al. Very little is known about proteins targeted by plant OGTs. However, protein overlay assays and coimmunoprecipation experiments allowed Taoka et al. Moreover, O-glycosylation with terminal GlcNAc modification has been described for nuclear pore complex proteins of tobacco, but, in contrast with typical O-GlcNAcylations, the modifications were oligosacharides rather than single O-GlcNAc residues Heese-Peck et al. Several proteins from different animal and human viruses have been shown to be O-GlcNAcylated Benko et al. In this paper, we identify one serine and seven threonine residues that are modified or influence the modification of other residues, and demonstrate that mutating the seven threonine residues to alanine blocks PPV CP modification. We also demonstrate that the non-modifiable mutant and wild-type PPV are similarly infectious to sec plants indicating that modification of host proteins has little or no role in the infection process. Finally, we present evidence that unmodified CP is more sensitive to proteases suggesting O-GlcNAc modification might affect virion structure. Mutational mapping using a heterologous E. Since the modifications made by SEC in E.

Chapter 2 : CFM International CFM56 - Wikipedia

This book advocates a new approach to safety and provides practical guides to safety practitioners that can be deployed directly on the shop floor. Based on his extensive experience with Los Alamos National Laboratory, Todd Conklin presents a human performance approach to safety drawing upon recent.

Abstract Exposure to ionizing radiation during childhood markedly increases the risk of developing papillary thyroid cancer. We examined tissues from 26 Ukrainian patients with thyroid cancer who were younger than 10 years of age and living in contaminated areas during the time of the Chernobyl nuclear reactor accident. We identified nonoverlapping somatic driver mutations in all 26 cases through candidate gene assays and next-generation RNA sequencing. We found that 22 tumors harbored fusion oncogenes that arose primarily through intrachromosomal rearrangements. Fusion oncogenes were less prevalent in tumors from a cohort of children with pediatric thyroid cancers that had not been exposed to radiation but were from the same geographical regions. Introduction There is strong epidemiological evidence that ionizing radiation is the triggering event leading to development of papillary thyroid cancers PTCs in children who were exposed to fallout after the Chernobyl nuclear reactor accident 1 , 2. The association between radiation exposure and generation of recombination events is likely direct and causal. The gene loci involved in these fusion events lie in close spatial proximity to one another within the human thyroid nucleus during interphase and are likely predisposed to recombination of adjacent chromosomal regions after radiation-induced DNA damage 9 , The role for radiation in generating fusion oncogenes in thyroid cells prompted us to screen a large number of post-Chernobyl cancer specimens to identify yet undiscovered driver translocations in this disease. We succeeded in identifying driver events in every case, including novel fusions that predict for alternative mechanisms of thyroid cell transformation. Results Screening for known genetic events in radiation-exposed pediatric thyroid cancer reveals a high prevalence of fusion oncogenes. We obtained tissue samples from 26 Ukrainian patients who were less than 10 years old and living in contaminated areas at the time of the Chernobyl accident to identify likely somatic oncogenic drivers of the disease Supplemental Table 1; supplemental material available online with this article; doi: We first screened them for known oncogenic events 4 , 11 â€” 13 and found driver mutations in tumors of 21 out of 26 patients: Five radiation-exposed thyroid tumors had no known driver alterations identified by this candidate gene approach and were therefore selected for paired-end RNA sequencing RNA-seq. Figure 1 Screen for genetic alterations in radiation-exposed pediatric thyroid cancer. C Summary of genetic alterations found in 26 radiation-exposed pediatric thyroid cancers. All but 5 harbored one of the previously described oncogenic events. The 5 tumors with no identifiable defect on the candidate gene screen underwent RNA-seq. Detection of novel fusion oncogenes in radiation-exposed pediatric thyroid cancer by RNA-seq. We generated an average of million reads for each sample and aligned them to the human genome hg19 using TopHat, which showed consistently high base quality on mapped reads and gene coverage for all samples Supplemental Figure 1. After stringent filtering for read depth and unique matching, we detected 16 somatic fusions that were tumor specific Supplemental Table 2. For each putative fusion we looked for reads supporting the inverse fusion e. We identified 3 somatic fusions in 4 out of 5 samples with likely oncogenic properties: The tumor harboring this fusion in our cohort showed a 3. Cells were depleted of serum for 24 hours prior to collection. The distribution of green fluorescence overlaps but does not colocalize with that of MitoTracker red. Expression of the oncoprotein promoted growth of NIH-3T3 cells in low serum and colony formation in soft agar Figure 2 C. These 2 genes are kb apart in the opposite orientation at 7q Exons 1 and 2 of AGK encode for the mitochondrial localization domain of the protein. Consistent with this, the fusion protein localized to the periphery of mitochondria Figure 3 E. This identified a somatic missense mutation, c. This mutation substitutes a serine for an isoleucine in codon p. SI within transmembrane domain 1 of this G proteinâ€”coupled receptor Figure 4. Activating mutations of TSHR stimulate thyrocyte proliferation and expression of thyroid differentiation genes. Accordingly, the tumor with the TSHR p. SI allele had markedly increased expression of thyroid-specific genes, including SLC5A5 also known as NIS , whereas all other

tumors showed predominant downregulation of this genetic program Figure 4 D. We also examined the RNA-seq data of the tumor samples from the radiation-exposed patients for all other somatic mutations and indels Supplemental Table 3 but did not identify other potential driver genetic abnormalities that may have contributed to radiation-induced thyroid tumorigenesis, indicating that a fairly small set of genetic aberrations likely account for tumor induction in most thyroid cancers. D Increased expression of genes required for thyroid differentiated function and thyroid hormone biosynthesis is restricted to the tumor with the activating TSHR. Gene expression analysis of RNA-seq data shows transcriptome signatures associated with the underlying oncogenic driver mutations. We next used a previously validated MAPK expression signature to determine which of the tumors analyzed by RNA-seq had induction of this pathway The tumor with the PPARG rearrangement showed expression changes consistent with a PPARG-driven transcriptional program 20 , underscoring the likely role of these genetic alterations as driver events in these tumors. Sporadic pediatric thyroid cancers have lower prevalence of fusion oncogenes. We next analyzed 27 sporadic pediatric thyroid cancers from the same geographical region that were carefully matched for age and tumor size Supplemental Table 1. We then screened these tumors for all known genetic alterations, including the novel fusions identified in the radiation-exposed cohort. The prevalence of driver fusions in tumors from this patient cohort was significantly different from that seen in the radiation-exposed group sporadic [9 out of 27] vs. Figure 5 Genomic landscape of PTCs from children exposed to radiation. A Summary of genetic alterations found in radiation-exposed left; T1â€”T26 and sporadic right; T27â€”T53 pediatric thyroid tumors. B Circos plot of rearrangements detected in radiation-exposed cancers. Breakpoints were assumed to lie in the middle of the introns immediately upstream and downstream of the fused exons, respectively. Rearrangements were color coded as follows: The thickness of the lines indicates the frequency of the fusion. Intrachromosomal rearrangements were the most prevalent events. Pathological characteristics of pediatric thyroid tumors correlate with driver alterations. The pathological characteristics of the radiation-induced and sporadic cases appeared to correlate primarily with the nature of the underlying driver mutation, as shown in Table 1. Table 1 Pathological features of pediatric PTCs Low-pass whole-genome sequencing shows no difference in the number of somatic SNPs, indels, or chromosomal rearrangements between sporadic and radiation-exposed tumors. To obtain a fuller picture of the genomic landscape of the radiation-exposed and sporadic pediatric thyroid cancers, we performed low-pass whole-genome sequencing WGS of 10 tumors and matched normal pairs 5 radiation exposed and 5 sporadic , with an average coverage of 7 to 8 times each base in the genome was sequenced 7 to 8 times on average , and aligned the reads to the human genome hg Eight out of these ten patients had previously identified driver mutations that were found during screening for the known oncogenic events, and all were confirmed in the low-pass WGS data. The full list of somatic chromosomal rearrangements is shown in Supplemental Table 4. Thus, despite the higher prevalence of fusion oncogenes in the radiation-exposed cohort, the overall frequency of somatic rearrangements is not different between the 2 groups. Altogether, we found no difference in the average count of nonsynonymous somatic SNVs in the sporadic and radiation-exposed groups Discussion Exposure of children to ionizing radiation after the Chernobyl reactor accident in increased the incidence of clinically significant thyroid cancers dramatically compared with that seen in the same regions of Belarus and Ukraine prior to the accident. By , the incidence of childhood thyroid cancer had increased to 4 cases per , children per year compared with 0. The risk was greatest in those exposed at a very young age. The incidence of thyroid cancer in children born after returned to baseline levels, highlighting the likely causal role of radiation in the pathogenesis of the disease. The tumor samples chosen for genetic analysis in this study were carefully selected to maximize the likely association with radiation exposure by selecting patients from the contaminated regions who were exposed at a very young age most were less than 5 years old at the time of the accident and who had clinically significant disease. The spatial organization of the genome is now thought to be a key contributing factor to the generation of chromosomal translocations in cancer The rationale to select RNA-seq rather than whole-exome sequencing as the primary modality to screen for new oncogenic drivers was based on these factors and the consequent prediction that fusion oncogenes were likely to predominate in this particular patient population. This fusion kinase is found in congenital fibrosarcomas and in secretory breast cancers 23 but has not been

previously reported in thyroid cancer. ETV6 is a member of the ETS family of transcription factors, and, for unclear reasons, its gene is frequently involved in chromosomal translocations in cancer. The chimeric ETV6-NTRK3 gene found in thyroid cancers differs in potentially significant ways from the fusion found in breast cancers and fibrosarcomas. The absence of this domain in the breast and fibrosarcoma fusion protein dictates a requirement for concomitant activation of insulin receptor substrate 1 IRS1 by insulin-like growth factor 1 for downstream signaling and transformation. IRS1 is believed to associate with the C terminus of the fusion protein 25 , One of the radiation-exposed patient samples in this cohort harbored this defect, and another was found to express a BRAF fusion with AGK. Despite this aberrant subcellular localization, the BRAF kinase faced the cytosol and was competent for signaling and transformation. Two of the twenty-six radiation-exposed cases had PPARG fusions, adding these to the spectrum of alterations present in radiation-exposed patients. Consistent with reports in the literature, these were associated with follicular-patterned histological variants of PTC Activating mutations of TSHR and GNAS are common in autonomously functioning thyroid adenomas and far less frequently in carcinomas but have not been previously identified in radiation-induced cancers. Consistent with this finding, the follicular-variant PTC harboring the TSHR mutation had higher expression of thyroid differentiation markers regulated by TSH signaling via adenylyl cyclase. Although the criteria used to select cases in this study were designed to obtain a cohort enriched for radiation-associated cancers, we accept that one or more sporadic cases may have been intermingled with this set. The only TSHR mutant case we found is insufficient to claim an association with radiation exposure. The prevalence of driver fusion oncogenes in tumors of the cohort with sporadic cases was much lower than that in the radiation-exposed group and consistent with that seen in children and adolescents from other geographical regions These data challenge the notion that fusion oncogenes are about equally prevalent in pediatric thyroid cancers, regardless of whether or not they are radiation induced. This led us to test the hypothesis that the overall genomic landscape of cancers from these two classes of tumors would also differ. Interestingly, the low-pass WGS of representative samples from the 2 groups failed to identify differences in the average number of somatic SNPs, indels, or rearrangements. The underlying predisposing factor s leading to development of sporadic pediatric thyroid cancers is not known. The relatively high frequency of passenger recombination events that they harbor suggests that there may be some deficit in DNA repair. Although radiation also leads to a high frequency of recombination events, the mechanisms accounting for these are likely to differ and may explain the higher likelihood of generation of fusion oncogenes. In conclusion, we identified nonoverlapping driver alterations for each one of the 26 radiation-exposed cases studied, highlighting the power of RNA-seq to reveal such alterations. At least 14 of these resulted from intrachromosomal rearrangements, lending further support to the evidence that spatial proximity favors generation of recombination events after radiation exposure and DNA damage 9 , Although the signaling pathways activated by the fusion oncogenes are similar to those engaged by the oncogenic drivers of thyroid cancers from adult patients, the spectrum of lesions is quite different, which may account for the differences in their biological and clinical behavior. The driver events found in radiation-exposed children arise within a mutational landscape induced by radiation damage, which underscores the need for rapid responses to mitigate the consequences of radiation exposure in children to avoid generation of oncogenic fusions that lead to increased risk of thyroid cancer. All radiation-exposed patients were from regions of Ukraine close to the Chernobyl nuclear reactor Supplemental Table 1 and were less than 10 years old in April 24 out of 26 were less than 5 years old. Patients were considered not to have been exposed if they were born after and were from the same geographical regions. All primary tumors were at least 1 cm in size. Detection of known fusion oncogenes and point mutations The cDNA of the 53 tumors was screened for recombination events previously described in PTC After ligation of the paired-end adapter, the to bp fraction was gel purified and amplified with 15 cycles of PCR. The resulting libraries were subjected to paired-end sequencing of bp reads on HiSeq Illumina. Bioinformatic analyses We used Snowshoes v2. A more detailed description is provided in the Supplemental Methods.

Chapter 3 : Pratt & Whitney J75 - Wikipedia

This article provides an introduction to the history of eugenics and explores the ways in which public history is particularly well suited to shape the historical memory of eugenics and encourage dialogue about contemporary biotechnologies.

Snecma, who had mostly built military engines until then, was the first company to seek entrance into the market by searching for a partner with commercial experience to design and build an engine in this class. The two companies saw mutual benefit in the collaboration and met several more times, fleshing out the basics of the joint project. GE needed an engine in this market class, and Snecma had previous experience of working with them, collaborating on the production of the CF turbofan for the Airbus A GE was initially considering only contributing technology from its CF6 engine rather than its much more advanced F engine, developed for the B-1 Lancer supersonic bomber. The project, and the export issue associated with it, was considered so important that French President Georges Pompidou appealed directly to U. President Richard Nixon in to approve the deal, and Henry Kissinger brought the issue up with President Pompidou in a meeting. Nixon administration officials feared that this project could be the beginning of the end of American aerospace leadership. Discussions at this meeting resulted in an agreement that allowed the development of the CFM56 to proceed. Contemporary reports state that the agreement was based on assurances that the core of the engine, the part that GE was developing from the military F, would be built in the U. The venture was officially founded in CFMI was made responsible for the day-to-day decision making for the project, while major decisions developing a new variant, for example required the go-ahead from GE and Snecma management. While work proceeded smoothly, the international arrangement led to unique working conditions. For example, both companies had assembly lines, some engines were assembled and tested in the U. The Snecma components the fore and aft sections of the engine were brought into the room, GE employees mounted them to the core, and then the assembled engine was taken out to be finished. The second engine was then shipped to France and first ran there on 13 December These first engines were considered "production hardware" as opposed to test examples and were designated as the CFM, the first variant of the CFM This engine had a slightly different configuration with a long bypass duct and mixed exhaust flow, [nb 1] rather than a short bypass duct with unmixed exhaust flow. The main targets were re-engine contracts for the Douglas DC-8 and the Boeing airliners, including the related military tanker, the KC Stratotanker. There was little initial interest in the engine, but Boeing realized that the CFM56 might be a solution to upcoming noise regulations. The new variant was listed as the The new engines are CFM high-bypass turbofans. Like other aspects of the program, international politics played their part in this contract. By the end of the s, airlines were considering upgrading their aging Douglas DC-8 aircraft as an alternative to buying new quieter and more efficient aircraft. The wings were closer to the ground than previous applications for the CFM56, necessitating several modifications to the engine. The program focused on developing a large number of new technologies for the theoretical future engine, not necessarily creating an all-new design. Launched in , the package included redesigned high-pressure compressor blades, an improved combustor, and improved high- and low-pressure turbine components [30] [31] which resulted in better fuel efficiency and lower nitrogen oxides NOx emissions. CFMI also offers the components as an upgrade kit for existing engines. Airbus As were to use this engine version starting in late

Chapter 4 : Criminal Investigations & Forensic Science

If the address matches an existing account you will receive an email with instructions to reset your password.

The sheath folds are steeply SSW-plunging closed structures whereas the cross folds are northâ€”south-oriented with near-horizontal fold axes. In the area south of Messina this complexly folded terrain grades continuously towards the south into a crustal-scale ENEâ€”WSW-trending ductile shear zone with moderate dip towards the WSW. All sheath folds document consistent top-to-the-NE thrust movement of high-grade material. Cross folds deform the S2 fabric and are characterized by a near-vertical axial planar cleavage S3. Mineral chemistry for metapelites from this cross fold shows a single peak on an NMg histogram for garnet reflecting a single phase of mineral growth. The progress of the two divariant retrograde reactions leads to the consumption of Grt and Fsp: K-feldspar Or94â€” never occurs with both cordierite and garnet. Microprobe profiling coupled with calculated isopleths for Bt, Grt and Crd in divariant equilibria define a decompression-cooling Pâ€”T path that reflects a single M3 high-grade metamorphic event during the evolution of the cross fold. Van Reenen et al. Mason was the first to subdivide the complex into three tectonic units: Most workers agree that the two marginal zones were exhumed and emplaced in the Late Archaean. The age of the formation and Pâ€”T history of the CZ is still being debated. Published data can therefore be interpreted to suggest that the deformational pattern of the CZ, dominated by two major folded structuresâ€”cross folds and sheath folds Figs 1 and 2 â€”reflects a major high-grade deformational event, either in the Late Archaean Hofmann et al. New age data Boshoff, , however, are not in accordance with the formation of the CFZ as the result of a single geodynamic event. Important sheath folds Avoca and Belleview and cross folds Baklykraal and Campbell are highlighted and the location of Fig. The thermodynamic Pâ€”Tâ€”fluid history of the CZ is also still the subject of debate. In addition, none of these studies integrated detailed structural data with the proposed Pâ€”T trajectories. In contrast, structural, metamorphic and physicochemical studies of major structures in the SMZ Smit et al. The aim of this paper is twofold: We use the following mineral abbreviations and thermodynamic symbols.

Chapter 5 : JCI - Identification of kinase fusion oncogenes in post-Chernobyl radiation-induced thyroid can

investigations that involve the study of constant velocity (Part I), constant acceleration (Part II), and projectile motion (Part III), which simultaneously involves constant velocity horizontally and constant acceleration vertically.

This article is a gentle introduction to differentiation, a tool that we shall use to find gradients of graphs. It is intended for someone with no knowledge of calculus, so should be accessible to a keen GCSE student or a student just beginning an A-level course. There are a few exercises. Where you need the answer for later parts of the article, solutions are provided, but you are strongly encouraged to try the questions as you go: Use the solutions to check your answers, rather than to avoid doing the questions! For example, in the graph above we can work out the gradient of each straight line section. But what if they were travelling at varying speeds? To find the gradient at a particular point, we need to work out the gradient of the tangent to the graph at that point - that is, the gradient of the straight line that just touches the graph there. Note that a straight line has the same gradient all the way along, whereas a curve has a varying gradient; we find the gradient at some specified point. But actually trying to draw this tangent is both fiddly and inaccurate. What would be really useful would be a more precise way of working out the gradient of a curve at a particular point. We have such a formula when the curve is a straight line: The idea of differentiation is that we draw lots of chords, that get closer and closer to being the tangent at the point we really want. By considering their gradients, we can see that they get closer and closer to the gradient we want. Have a go with the following interactivity to see what I mean. If you can see this message Flash may not be working in your browser Please see http: Do you agree that if we could work out the gradients of different chords as they approximate the tangent better and better, and if they tend to a limit , then we could work out the gradient of the tangent? By "tend to a limit", I mean that they get closer and closer, and in fact get as close as we like. But can we actually use it? Try several different points, and see whether you can spot a pattern. So far, so good. And I never got my pencil and ruler out to actually draw some tangents! Exercise 2 How does this answer compare with your experimentation in Exercise 1? Are you happy with this? Exercise 5 Compare this answer with your experimentation in Exercise 3. Exercise 8 Draw up a table like this one:

Chapter 6 : Amplitude Modulation

Chapter 11 Limits and an Introduction to Calculus The Limit Concept The notion of a limit is a fundamental concept of calculus. In this chapter, you will learn how to evaluate limits and how they are used in the two basic problems of calculus: the.

Chapter 7 : An Introduction to Differentiation : calendrierdelascience.com

This article is a gentle introduction to differentiation, a tool that we shall use to find gradients of graphs. It is intended for someone with no knowledge of calculus, so should be accessible to a keen GCSE student or a student just beginning an A-level course.

Chapter 8 : O-GlcNAc modification of the coat protein of the potyvirus Plum pox virus enhances viral infecti

Physica Scripta. Vol. T53, , Radiofrequency Electron Swarm Transport in Reactive Gases and Plasmas K. Maeda and T. Makabe Department of Electrical Engineering, Faculty of Science and Technology, Keio University, Hiyoshi, Yokohama Japan.