

1: The Paston Letters, A.D. V3 (): James Gairdner: www.enganchecubano.com: Books

A collection of the chronicles and ancient histories of Great Britain, now called England From A.D. to A.D. -- v. 3. From A.D. to A.D.

CollectCollect this now for later debra Catherine of France 27 October 1439 3 January 1492 was the Queen consort of England from until It was through her second marriage to Owen Tudor that created the Tudor line. His other legitimate descendants included, by his first wife, Blanche, his daughters Queen Philippa of Portugal and Elizabeth, Duchess of Exeter; and by his second wife, Constance, his daughter Queen Catherine of Castile. Grandmother to Mary, Queen of Scots. It is believed that Blanche may have died aged 22 after contracting the Black Death which was rife in Europe at that time. Owain ap Maredudd ap Tewdwr and his wife Catherine of Valois. They were the parents of Edmund Tudor and the paternal great-grandparents of Prince Arthur and his siblings. She was present when her husband was assassinated in 1415, and was also a target. She was injured but managed to escape, assuming the regency for her young son, James II. She was the great, great grandmother of Mary, Queen of Scots. Considered by many to be the greatest monarch in English history. Elizabeth I 1533 1548 was queen regnant of England and Ireland from until her death. Elizabeth was the fifth and last monarch of the Tudor dynasty. The daughter of Henry VIII, she was born a princess, but her mother, Anne Boleyn, was executed two and a half years after her birth, and Elizabeth was declared illegitimate. When all the family intrigue and in-fighting was said and done, she prevailed and became successor to the Crown. Favorites CollectCollect this now for later margery St. In 1554, Mary Tudor signed the treaty surrendering Calais at the Palace. She was almost as powerful as her husband, who specified in his will that she was to rule alongside their son in the event of his death. Favorites CollectCollect this now for later natalie-w The Battle of Bosworth Field was the last significant battle of the Wars of the Roses, the civil war between the Houses of Lancaster and York that raged across England in the latter half of the 15th century. The battle was won by the Lancastrians. As is the case with many of the medieval queens consort of the Kingdom of England, relatively little is known of her life. In 1527, she also held the position of Ambassador for the Spanish Court in England when her father found himself without one, becoming the first female ambassador in European history. Her old husband, the King of France, died and he was supposed to bring her home to England. They fell in love and got married instead! Second wife of King John. Queen from 1192 - King John divorced his first wife, Isabel of Gloucester, to marry Isabella. She had many children with him, including the future Henry III. After his death she remarried Hugh X of Lusignan, who was supposed to marry her daughter Joan, but jilted the girl to marry her mother. She had several more children with him. She was the mother of king Amenhotep I and may have served as his regent when he was young. Ahmose-Nefertari was deified after her death.

2: Taylor v. O'GRADY, F. Supp. (N.D. Ill.) :: Justia

A collection of the chronicles and ancient histories of Great Britain, now called England / by John de Wavrin, lord of Forestel, translated by William Hardy. [V. 3] From A.D. to A.D.

Jackson, individually and on behalf of all others similarly situated, Plaintiffs, v. United States District Court, N. This is a civil rights class action, on behalf of the class of correctional officers and supervisors at the Cook County Department of Corrections "DOC" , challenging the constitutionality of a compulsory urine testing program. The program compels all correctional employees, on pain of termination, to submit urine specimens for the purpose of drug testing. An employee must submit a urine sample in the absence of a reasonable suspicion that the employee is illegally using drugs. The named plaintiffs, Yvonne L. Taylor, Charles Edwards, and Jean S. Jackson, are currently employed as correctional officers with the Department of Corrections. Also named as a plaintiff is Frankie McNeal, a correctional sergeant and supervisor. Acting pursuant to their responsibilities, defendants have ratified and implemented General Order 9. The complaint seeks certification of the class of correctional employees and supervisors at the Department of Corrections "DOC". In a previous order, I certified the class to include all correctional employees and supervisors at the DOC, except for the defendants and those employees of the DOC who testified for the defendants. Further, the complaint seeks a declaration that the follow-up compulsory tests for those who test positive initially be declared violative of the fourth amendment. Relatedly, the complaint seeks a declaration that the continued employment of correctional employees may not be conditioned on their willingness to consent to mandatory urine testing. Finally, the complaint requests that defendants be permanently enjoined from implementing and enforcing the urine testing program described by General Order 9. See *National Federation of Federal Employees v. [redacted]*. Accordingly, I held a full trial on the merits over several days. Having heard testimony from several expert and non-expert witnesses on the scope of and need for the program of compulsory urinalysis of all employees, I now make my findings of fact and conclusions of law in accordance with Fed. It may be summarized as follows. Once annually every correctional employee, no matter of what rank, will be compelled to submit a urine specimen for chemical urinalysis. The correctional officer to be tested will not be advised of the pendency of the test until roll call on the day on which the specimen is to be submitted. There are two situations in which an officer may be compelled to submit a urine specimen more than once annually. First, if the officer has already submitted a urine specimen which tested positive, and the officer has elected to enter a drug counseling and treatment program, the officer will be tested twice monthly for a period of six months. Second, if, in the view of a correctional superintendent or higher officer, there is a reasonable and articulable suspicion that an officer is using drugs illegally, is in possession of illegal drugs, or is bringing drugs into the institution, he or she will be tested. The actual procedure for eliciting urine from the employees and chemically analyzing the urine samples is as follows. The employee is notified at roll call at the beginning of her or his shift that the test is to take place. The employee is then taken to the holding area for urinating and is required to wait there until able to urinate. The employee has the balance of the shift to provide her or his urine specimen. The purpose of this inquiry is informational. In the event that there is a positive test result, the employee will not appear to have recently fabricated a defense to a prospective charge of drug use. After the employee has provided the medical information, or indicated that she or he declines to provide it, the employee will be taken to the appropriate washroom. Prior to the entry of the employee into the washroom, the investigator administering the test will inspect the washroom to assure that there are not articles present which could impair the test. After doing so, the investigator will then conduct a "pat down" search of the employee for the same purpose. The standard "pat down" search consists of the visual observation of the person searched and lightly patting or running the hands over the body extremities and torso to assure that there are no objects present which may be used to corrupt the specimen. The correctional officer urinates in a cup provided for that purpose. The procedure is observed generally by the assigned investigator from a "discreet" distance. The actual physical observation of the flow of urine from the body into the cup is not required or recommended, unless the investigator is possessed of facts which indicate that the person giving

the sample is going to attempt to impugn the veracity of the test by switching samples, substituting water for urine, or the like. Under ordinary circumstances, therefore, women can be in a stall with the door closed, and men at a urinal with their back to the investigator. After the urine specimen has been obtained, it is placed in two containers and sealed. If the EMIT test shows a positive result for the presence of marijuana, cocaine, heroin, or opiates the only drugs being tested for, the opened sample is resealed and, together with the unopened sample, is sent to the Met-Path Laboratories for a confirmation examination utilizing the Gas Chromatography-Mass Spectroscopy Method "GCMS". In the event that the results of the EMIT test are confirmed, the employee will be informed of her or his option to have a second GCMS test performed upon the given urine sample by a reputable laboratory. If this test fails to confirm the positive test results already obtained, no action will be taken against the employee. If the employee chooses not to do so, the Sheriff will file a complaint with the Cook County Police and Corrections Merit Board seeking termination of the employee. If the employee chooses to enter the drug treatment program, she or he will be compelled to submit two urine samples per month for six months to assure that the employee is not continuing to ingest drugs. Positive test results during the treatment program, or positive test results at a later date after completion of the program, will result in the Sheriff seeking the termination of the employee before the Cook County Police and Corrections Merit Board. At any time, the failure to provide a urine sample when directed to do so is grounds for termination.

The Interests the Government Seeks to Protect The defendants advanced three interests which they believe will be promoted through this program of urine testing: The defendants instituted the current drug testing program primarily out of their first interest in countering what they perceived to be the problem of correctional officers smuggling contraband into the prison facility. The other two interests, however, also factored into their decision to implement and ratify the testing program. Evidence of Substance Abuse and Drug Trafficking The evidence presented at trial on the nature of substance abuse alcohol and drug, legal and illegal and the extent of the problem came in two forms. First was the testimony of Dr. Schnoll testified, among other things, to the extent of the problem of drug and alcohol abuse in society. These exhibits contain reports of various types of drug related problems at the DOC from through April, Fifty-six of these reports involve allegations that correctional officers were handling illegal drugs. Twenty-seven involve arrests for suspected drug possession off duty; three involve cases where the officer was found in suspected possession inside the DOC; twenty-six involve inmate or anonymous allegations that correctional officers were trafficking drugs in the DOC. The remaining two-thirds of the reports describe cases where inmates were found in possession of drugs, drugs were found somewhere in the institution such as in clothing intended for inmates or mail intended for inmates, or drugs were found on visitors of inmates. Throughout the trial it was agreed that these reports were not admitted for the purpose of the truth of the allegations asserted therein. Both parties acknowledged that the purpose of admitting these reports was only to establish, confirm or clarify the state of mind of the witnesses who read some or all of these reports Glotz and Hardiman. The acknowledgment that these reports were admitted for this limited purpose is well founded. The substance of every single report was hearsay. Of the fifty-six reports involving correctional officers, only two of them indicate that a criminal judgment of conviction was entered against the officer. These two convictions were for possession of drugs off duty. The remaining cases either do not indicate the criminal disposition, or indicate that the charges are still pending or were dismissed. Many of these reports also indicate how the DOC investigator who conducted an internal investigation disposed of the charges. Some charges were sustained, some dismissed, and some suspended. Nevertheless, as all parties and I expressly agreed at trial, these reports were not admitted for their truthfulness. Thus, as indicated before, I regard them as merely providing evidence for and clarification of the subjective state of mind of those who read them. Since Glotz and Hardiman read Groups A and B, respectively, I find that, consistent with their testimony, they in fact believed there to be a drug problem involving correctional officers at the DOC. I do not and cannot regard the reports themselves as tending to show that a drug problem involving correctional officers in fact exists at the DOC, or what the nature of that problem is, since, as just explained, those reports were not admitted for their truth. I also find that Dr. While his testimony pertained to the drug problem in society generally, there was no evidence suggesting that the subpopulation of correctional officers was worse than the overall population. Schnoll also

testified that the drugs most commonly abused, aside from alcohol, are legal drugs such as prescription drugs, sleeping pills, and sedatives. Finally, Schnoll explained that in his opinion, after reviewing reports from the National Institute on Drug Abuse and his own observations and work, under one-tenth of those who use illegal drugs are "chronic" drug users. In his testimony, Dr. Schnoll defined a chronic drug user as one who uses drugs on a regular basis, usually three or four times a week, and displays addictive and sometimes desperate behavior. There are approximately correctional officers and supervisors at the DOC. For purposes of making a calculation, I can assume that Dr. Of course, the urine testing program, testing as it does for cocaine, heroin or opiates, and marijuana, would not detect members of this last and obviously largest group. There is no evidence contrary to these numbers. Hardiman estimated that between and about to correctional employees had substance abuse problems. He also explained how he arrived at this figure. As just stated, there are about correctional employees at any one time. This is people. He then explained that he had to factor in an additional number of substance abuse cases because of attrition and new hires over the six year period. Thus, he revised his estimate upward from to to employees. Rather, Hardiman merely had to adjust that one-time estimate upward to determine the number of employees with abuse problems over a six year period. Three of the ninety-four reports in Exhibit B indicate that a correctional officer was found in possession of a suspected illegal drug while on duty. Twenty-three of the reports involve allegations some dismissed of off-duty possession. Thirty involve allegations by an inmate or an anonymous person that a correctional officer was trafficking in drugs. However, only in four of these trafficking cases did the DOC investigator actually sustain the charges. As Hardiman explained at trial, "[w]e get a lot of reports from inmates on officers Inmates are likely to report officers for no reason at all The remaining thirty-eight cases in Exhibit B involve problems with inmates and drugs, drugs in inmate mail, and visitors with drugs. Indeed, as indicated above, the Sheriff willingly assumed that the drug problems at the DOC were similar to the population at large. While he labeled the DOC drug problem "serious," he did not quantify this and expressly refrained from calling it "extremely serious. All of them involved allegations of drug smuggling into the jail, and they were all currently under investigation. He knew that two of the reports involved only individuals; he did not know how many were involved in the other two investigations. This label, of course, is not a quantification. There is a difference.

Add tags for "A collection of the chronicles and ancient histories of Great Britain, now called England / [3].From A.D. to A.D. ". Be the first.

This section needs additional citations for verification. Please help improve this article by adding citations to reliable sources. Unsourced material may be challenged and removed. June Main article: He was born on 6 December at Windsor Castle. His mother, Catherine of Valois , was then 20 years old. On 28 September , the nobles swore loyalty to Henry VI. His duties were limited to keeping the peace and summoning Parliament. After the Duke of Bedford died in , the Duke of Gloucester claimed the Regency himself, but was contested in this by the other members of the Council. It was shortly after his crowning ceremony at Merton Priory on All Saints Day, 1 November , [5] shortly before his 16th birthday, he obtained some measure of independent authority on 13 November , [6] but his growing willingness to involve himself in administration became apparent in when the place named on writs temporarily changed from Westminster where the Privy Council was to Cirencester where the king was. Henry was declared of age in , at the age of sixteen in the year in which his mother died, and he assumed the reins of government. Henry, shy and pious, averse to deceit and bloodshed, immediately allowed his court to be dominated by a few noble favourites who clashed on the matter of the French war. The young king came to favour a policy of peace in France, and thus favoured the faction around Cardinal Beaufort and William de la Pole, Earl of Suffolk , who thought likewise, while Humphrey, Duke of Gloucester , and Richard, Duke of York , who argued for a continuation of the war, were ignored. In , the English council suggested that peace could best be effected with the Scots by wedding Henry to one of the daughters of the king of Scotland ; the proposal came to nothing. During the congress of Arras in , the English put forth the idea of a union between the English king and a daughter of Charles VII of France , but the Armagnacs refused to even contemplate the suggestion unless Henry renounced his claim to the French throne. These conditions were agreed to in the Treaty of Tours in , but the cession of Maine was kept secret from parliament, as it was known that this would be hugely unpopular with the English populace. However, Margaret was determined to make him see it through. As the treaty became public knowledge in , public anger focused on the Earl of Suffolk, but Henry and Margaret were determined to protect him. Queen Margaret had no tolerance for any sign of disloyalty towards her husband and kingdom, thus any inclination of it was immediately brought to her attention. Gloucester was put in custody in Bury St Edmunds , where he died, probably of a heart attack although contemporary rumours spoke of poisoning before he could be tried. However, he was excluded from the court circle and sent to govern Ireland , while his opponents, the Earls of Suffolk and Somerset were promoted to Dukes , a title at that time still normally reserved for immediate relatives of the monarch. His murdered body was found on the beach at Dover. By , the French had retaken the whole province, so hard won by Henry V. Returning troops, who had often not been paid, added to the lawlessness in the southern counties of England. Jack Cade led a rebellion in Kent in , calling himself "John Mortimer", apparently in sympathy with York, and setting up residence at the White Hart Inn in Southwark the white hart had been the symbol of the deposed Richard II. The flight proved to have been tactical: Cade successfully ambushed the force in the Battle of Solefields and returned to occupy London. In the end, the rebellion achieved nothing, and London was retaken after a few days of disorder; but this was principally because of the efforts of its own residents rather than the army. At any rate the rebellion showed that feelings of discontent were running high. Insanity, and the ascendancy of York[edit] Depiction of Henry enthroned, from the Talbot Shrewsbury Book , 1455 In , the Duke of York was persuaded to return from Ireland, claim his rightful place on the council and put an end to bad government. His cause was a popular one and he soon raised an army at Shrewsbury. The court party, meanwhile, raised their own similar-sized force in London. A stand-off took place south of London, with York presenting a list of grievances and demands to the court circle, including the arrest of Edmund Beaufort, 2nd Duke of Somerset. The king initially agreed, but Margaret intervened to prevent the arrest of Beaufort. By , his influence had been restored, and York was again isolated. The court party was also strengthened by the announcement that the Queen was pregnant.

However, on hearing of the final loss of Bordeaux in August, Henry experienced a mental breakdown and became completely unresponsive to everything that was going on around him for more than a year. Henry may have inherited a psychiatric condition from Charles VI of France, his maternal grandfather, who was affected by intermittent periods of insanity during the last thirty years of his life. York was named regent as Protector of the Realm in 1422. There followed a violent struggle between the houses of Lancaster and York. Henry was defeated and captured at the Battle of Northampton on 10 July. By this point, however, Henry was suffering such a bout of madness that he was apparently laughing and singing while the battle raged. Edward failed to capture Henry and his queen, who fled to Scotland. Henry, who had been safely hidden by Lancastrian allies in Scotland, Northumberland and Yorkshire, was captured by King Edward in 1423 and subsequently held captive in the Tower of London. While imprisoned, Henry did some writing, including the following poem: Kingdoms are but cares, State is devoid of stay, Riches are ready snares, Pleasure is a privy prick Which vice doth still provoke; Poms, imprompt; and fame, a flame; Power, a smoldering smoke. Who meant to remove the rock Owst of the slimy mud Shall mire himself, and hardly scape The swelling of the flood. By herself, there was little she could do. However, eventually Edward IV had a falling-out with two of his main supporters: However, by this time, years in hiding followed by years in captivity had taken their toll on Henry. Warwick and Clarence effectively ruled in his name. Warwick soon overreached himself by declaring war on Burgundy, whose ruler responded by giving Edward IV the assistance he needed to win back his throne by force. Official chronicles and documents state that the deposed king died on the night of 21 May. The common fear was the possibility of another noble utilizing the mentally unstable king to further their own agenda. When the body of the king was found several centuries later, diggers found it to be five foot and nine inches. Light hair had been found to be covered in blood, with damage to the skull, strongly suggesting that the king had indeed died due to violence.

4: Henry VI of England - Wikipedia

Recueil des croniques et anchiennes istories de la Grant Bretaigne, Å present nommÅ© Engleterre. 3. From A. D. to A. D. / par Jehan de Waurin, ; ed. by William Hardy.

A Peasant With Balls of Steel See entire painting at the end of this page. Who Was Joan of Arc? Joan was a very courageous young woman. She was a simple peasant girl and a strong believer. More to the point, she claimed that she was in tune with some of the Saints because they spoke to her. Joan was born in Domremy as well. Here is Domremy on a map. The Duchy of Bar became part of Lorraine in By then, of course, Joan was long gone. Today, the tiny village of Domremy is home to about residents. And here is a recent photo: Thus, Joan developed a strong patriotic sense. Check the map above to see how France was sandwiched by the English on the mainland and Burgundy. And here is more on the This painting shows Joan in her early days. We see her standing in the garden of her parents at that exact moment when The Voices made contact. Metropolitan Museum of Art Painter Jules Bastien-Lepage, himself hailing from Damvillers, Lorraine, received some harsh comments from the critics, who could not appreciate his mixture of naturalism and mysticism. Who were these voices, and what did they want? The voices, who revealed themselves as St. Michael main man , St. Catherine of Alexandria legendary young Christian girl, later martyr, struggling against persecution under the Roman emperor Maxentius in the 4th century , and St. Margaret of Antioch legendary virgin, later martyr, whom even the Devil himself could not digest [long story] , told Joan that she was to save France. So far, so good. As Joan grew older, the voices became more specific. They informed her that she was the instrument chosen by Heaven itself to drive away the English. Her mission, should she choose to accept it, was to bring the Dauphin to Rheims or Reims where he would become anointed king. Joan of Arc immediately notified her parents, packed her bundle, and was on her way. A dauphin, by the way, is the title of the eldest son of the King of France. This title was in use from to The people of Vaucouleurs were intrigued by young Joan, partly because of her piety and devoutness, partly because of her spunk and enthusiasm, but mostly because of her ability to tie all of the above together with patriotism that, frankly, was as solid as it was badly needed. Joan explained to the good citizens of Vaucouleurs that the voices had asked her to dress up as a knight. The townspeople were delighted and fell into competition with each other to equip the girl with the best horse, armor, and sword. Baudricourt himself arranged for an escort and a very sharp looking Joan was accompanied to the French town of Chinon where she was to meet the Dauphin Charles. Having arrived at Chinon, Joan was invited into a room full of people in fancy outfits. Among these people mingled Charles, whose attire was carefully selected to blend in perfectly. Nothing gave away his true identity. The idea was to see if Joan could identify the Dauphin, whom she never met before in her life, on her own, which would confirm that Heaven was in fact speaking French in general and through Joan of Arc in particular. Joan spotted and addressed Charles right away. While the entire audience was still trying to figure out how she done it â€” and briefly contemplated frisking her sleeves for potential flower bouquets â€” Joan kept on track and prompted Charles on his new agenda: He was to be crowned king in the city of Rheims. Joan had a private meeting with Charles before the big official first introduction and could therefore easily recognize him. Welcome to political stunts of the Middle Ages. Their lands were destroyed and their morale was shattered. But now that Providence had seemingly taken a breath mint, an invigorating wind of change blew across the land. A Holy Maid led the way, and France felt perky again. And then events happened with the quickness: Joan visited the French camp at Blois, and on April 25, , she left for Orleans, where she arrived on April Her courage and her loyalty to Charles VII. In September , Joan was severely wounded while trying to take Paris in the name of her king. Joan of Arc in Action Gutenberg Project.

About this Book Catalog Record Details. The Paston letters, A.D. New complete v View full catalog record. Rights: Public Domain in the United States, Google-digitized.

Proteins are uniquely capable of identifying targets with unparalleled selectivity, but, in addition to the precision of the binding phenomenon, nature has the ability to find its targets exceptionally quickly. Transcription factors for instance can bind to a specific sequence of nucleic acids from a soup of similar, but not identical DNA strands, on a timescale of seconds. This is only possible with the enhanced kinetics provided for by a natively disordered structure, where protein folding and binding are cooperative processes. The secondary structures of many proteins are disordered under physiological conditions. Subsequently, the disordered structures fold into ordered structures only when they bind to their specific targets. Induced folding of the protein has two key biological advantages. First, flexible unstructured domains can result in an intrinsic plasticity that allows them to accommodate targets of various size and shape. And, second, the dynamics of this folding process can result in enhanced binding kinetics. This review describes experimental results in rationally designed peptide systems where the folding is coupled to amphiphilicity and biomolecular activity.

Introduction Configurational dynamics in proteins have been found to be critical to a variety of physiological processes [1 , 2] such as transcription and translation regulation [3], cellular signal reduction [4], protein phosphorylation [5] and molecular assemblies [6]. The cooperative processes of folding and binding are important to many of these biological processes and include several intra- and inter-molecular factors that determine the interaction dynamics between the proteins and their targets [7]. This structural motif has been found to play multiple roles in protein folding, protein-protein recognition, protein-membrane interactions, and protein and peptide biological activity [8]. Designing biomimetic peptides from natural analogues requires a lucid perspective on naturally occurring protein folding and binding as cooperative processes [2 , 11 – 13], where the protein searches for favorable intramolecular or intermolecular interactions [14 – 16]. There are many proteins in nature that are disordered in their physiological condition, but when they bind to the specific target or site, they become more ordered [11 , 17 – 19]. This phenomenon of coupled folding to binding has been shown to enhance the binding kinetics and the selectivity of the overall binding process [16 , 20]. Induced folding of the protein results in key structural and thermodynamic changes. First, flexible unstructured domains with an intrinsic plasticity allow proteins to accommodate targets of various size and shape; and second, free energy of binding is required for compensation for the entropic cost of ordering of the unstructured region. A site that does not provide enough binding free energy cannot induce folding and, hence, cannot form stable complex. While the notion of induced folding provides a thermodynamic framework for the configurational changes associated with the binding of intrinsically disordered proteins, other efforts have examined the influence of kinetics on natively unfolded proteins. In this scenario, an unfolded protein binds weakly to its target site at a relatively large distance followed by the folding of the protein as it approaches the specific binding site. Engineering synthetic peptides with controllable molecular architectures that mimic the natural phenomena observed in this class of proteins requires careful consideration of the dominant inter- and intramolecular interactions. In the next section, we will examine several protein systems and biologically inspired peptide systems that have the ability to bind DNA and RNA, changing states from intrinsically disordered to ordered on binding. In the fourth section, we will discuss the ability to use these rules in combination with native binding sequences to engineer new amphiphilic peptide analogues.

DNA Binding Proteins A handful of researchers have attempted to use these intrinsically disordered proteins as the models for their peptide design, where peptides are constructed to mimic the dynamics of the binding process observed in nature. These authors are motivated to design peptides that explore the fundamental relationship between the dynamics of the folding and the kinetics of the selective binding that will lead to better understanding of the overall process. Such peptides with accelerated kinetics can be used for designing new a generation of molecules that can be used as rapid acting diagnostic tools. For example, the basic leucine zipper family bZIP , one of the best characterized family of DNA binding motif, consist of a N-terminal basic region

that binds to a specific sequence of DNA and C-terminal leucine zipper that is responsible for dimerization [23 – 25]. In the absence of DNA, leucine zipper is helical and dimeric while the basic region is flexible and partially disordered. In presence of sequence specific DNA, the basic region is fully helical, which shows that the folding of the protein is coupled with the binding of its target DNA. The activity of the transcription factor captures both aspects discussed in the prior section; the existence of the intrinsically disordered state yields enhanced kinetics fly-fishing , and conformational selection is exhibited on target binding. An induced helical fork model has been devised suggesting that the role of the leucine zipper is to position the basic region so that the zipper can both interact with DNA and promote the helix formation in the basic regions, where helicity is induced in basic region only in presence of the target DNA. The helical fork model also identifies the residues that are important for helix stability but do not help in DNA recognition. The authors also showed that the specificity is maintained as the binding with non-specific DNA does not show rise in helicity of basic region as compared to that with specific DNA. A peptide was synthesized with the basic region corresponding to the residues – of GCN4 and the leucine zipper was replaced with the Gly-Gly-Cys liner at the C-terminal. This peptide was then dimerized to give a disulphide-bonded dimer and, using DNase I footprinting, they showed that it retains the sequence specificity by comparing the results with the basic region attached to leucine zipper. The minimum length for the basic region sequence for specific binding was also determined [27 , 28]. Peptides of different sizes of basic region were synthesized with the GGC linker attached to give disulphide-bonded dimer after dimerization. DNase I experiments were conducted, and it was found that the peptides containing only 20 residues of GCN4 basic region show the same sequence specificity as that of intact protein. Also, circular dichroism experiments showed that 15 residues from the basic region of GCN4 – form a helix when contacting the specific DNA target. This sequence provides a template for peptide designs to study the interactions of a class of DNA-binding peptides where folding and binding are cooperative. Other authors have taken advantage of this inherent modularity of DNA-binding sequences, combining dimerization domains with DNA binding domains. This peptide sequence has been shown to bind specifically to Z-DNA [29]. The peptide amphiphiles enhance secondary structure and form hierarchical structures as they bind to DNA in helical conformation. Peptide amphiphiles, in general, are capable of forming hierarchical assemblies, making them an interesting choice to use as functional building blocks for different systems such as gene delivery and artificial transcriptional factors [31 , 32]. Binding of neuleolin protein with its cognate stem loop RNA induces folding of RNA hairpin loop and the ordering of the two RNA binding domains of the protein [37 , 38]. In another example, the Tobacco Mosaic Virus coat protein has a residue loop that is natively disordered but undergoes a disorder-to-order transition upon RNA binding during the assembly of the capsid [40 – 43]. Several authors have shown that Rev protein, an essential regulatory protein encoded by human immunodeficiency virus, has arginine-rich binding regions that are found in many viruses [44 – 46]. In this case, specific binding of Rev protein to RNA not only stabilizes the complex but there is a change in conformation of RNA [47]. At low temperatures, an increase in the helicity of Rev peptide is observed when it binds selectively to IIB RNA, which again suggest that the binding is coupled to the folding [48]. Additionally, the peptide is able to bind the Rev responsive element specifically and is sufficient for a high binding affinity, comparable to that of Rev [48 – 50]. The examples described above represent scenarios where researchers have used intrinsically disordered proteins as models for the design of their peptides. The motive behind the design of these peptides is to mimic the original protein, but engineering synthetic peptides that will mimic the dynamics observed in nature requires careful consideration of the dominant inter- and intra-molecular interactions. Defining the thermodynamics of secondary structure stability will help in understanding the structure-function relationship, leading to better understanding of the overall dynamics observed in nature. DeGrado and Lear study was based on the design of three synthetic peptides comprising of leucine L and lysine K with different hydrophobic periodicities and chain lengths. As all the three peptides consist of only two amino acids, leucine and lysine, intrinsic propensity for each peptide is the same and the only difference is the hydrophobic periodicity, and the effect of hydrophobic periodicity on the secondary structure can be investigated Table 2. Circular dichroism was used to measure the secondary structure in bulk, and Langmuir Blodgett technique was used to study the properties

of peptides at an air-water interface. Peptide conformation at the air-water interface was determined by compressing the peptide monolayers and transferring them to a solid substrate by using Langmuir Blodgett, and the secondary structure was detected by using infrared and circular dichroism spectroscopy. Langmuir Blodgett experiments showed that peptides B and C formed more stable monolayers as compared with peptide A. Due to hydrophobic periodicity, peptides B and C form a more stable secondary structure such that the hydrophobic residues are segregated on one side, forming an apolar surface Figure 3. At air-water interface, the apolar surface of the peptide will partition into air phase, where the free energy of dehydration of the hydrophobic side chains is the driving force for separation, stabilizing the amphiphilic secondary structure of the peptide. Each group has one hydrophobic residue, one negatively charged residue and one positively charged residue. Thus, there are two sets of peptides where the permutations intrinsic inclination versus periodicity can be explored. Their work corroborates the idea that periodicity of polar and non-polar residues dominates the secondary structure of the sequence. Stability of the secondary structure is also an important aspect in designing synthetic peptides. These experiments show that the synergistic effect of intrinsic propensities and hydrophobicity drives the formation of stable helices. This was proven by the LK peptides described above. Still, the activity of these amphiphilic sequences captures only one aspect discussed in the introduction, namely, conformational selection and not fly-casting. The following section discusses the potential to apply these dynamics to peptide design for selective binding, where one can create novel peptide sequences that have dynamic amphiphilicity by folding in response to environmental cues. Such a peptide with tunable amphiphilicity can be designed to bind to a wide range of targets, coupling dynamic amphiphilicity to selective binding. Moreover, these peptides can take advantage of the accelerated kinetics inherent in natively unfolded structures and applied as a template for next generation biologically inspired molecular designs.

Engineered Synthetic Peptides 4. Membrane Mimics

Amphiphilicity is an important characteristic of many membrane bound peptides and proteins such as apolipoproteins, peptide hormones, and signal peptides. A model docosapeptide is designed by equally distributing acidic and basic residues on the hydrophilic side and amino acids were selected such that the model peptide is different from the repeating Apo-I peptide sequence. Melittin, a toxic component from bee venom, is a hexacosapeptide in which the N-terminal region is predominantly hydrophobic residues 1-20 and C-terminal is predominantly hydrophilic residues 21-26 Figure 5B. The membrane interface has a potent ability to induce the secondary structure in melittin, and this folding of the peptide is coupled with its partitioning in the membranes. It has been shown that the amphiphilic structure is important for the hemolytic activity of mellitin [70]. Serine residues are included to increase the hydrophobicity of the model peptide such that the amphiphilicity is equivalent to native peptide. These synthetic analogous amphiphilic helical peptides of simple sequence are a powerful tool for the systematic study of the structure-function relationship of lipid-associated proteins and the construction of water-soluble lipid-peptide complexes of desirable physical and physiological properties. These results also suggest that the rational design of peptides based on secondary structure considerations is a useful tool to elucidate the structure-function relationship in biologically active peptides. Glutamic acid is selected as a titratable residue that destabilizes the helix while at low pH and promotes the helix formation at high pH. The hydrophobic face has enough hydrophobicity to interact with the neutral bilayer membranes at low pH [74 , 75]. There are several papers that investigate the mechanism of pore formation, rates of membrane permeabilization and the role of sequence [76 - 81]. LAGA peptide is designed from the same amino acids where the only difference is in the positioning of the leucines and glutamic acids figure 6. Therefore, the GALA peptide can initiate leakage of vesicle contents and membrane fusion [82].

6: Robert Cary (died c.) - Wikipedia

*The Paston Letters, A.D. V3 () [James Gairdner] on www.enganchecubano.com *FREE* shipping on qualifying offers. This scarce antiquarian book is a facsimile reprint of the original.*

7: Search for Information - Mississippi State Department of Health

V. 3. FROM A.D. 1422 TO A.D. 1431. pdf

A collection of the chronicles and ancient histories of Great Britain, now called England. 3. From A. D. to A. D. / by John de Wavrin, lord of Forestel ; transl. by William Hardy, and Edward L. C. P. Hardy.

8: MARE, Robert de la (c), of Aldermaston, Berks. | History of Parliament Online

The Paston letters, A.D.: a reprint of the edition of , which contained upwards of five hundred letters, etc., till then unpublished, to which are now added others in a supplement after the introduction.

9: The Paston Letters, A.D. Series by James Gairdner

Chronicon rerum gestarum in Monasterio S. Albani a quodam auctore ignoto compilatum (A.D.). Annales Monasterii S. Albani a Johanne Amundesham conscripti--v. 2.

Musicophilia tales of music and the brain Libretto of Djakh and Djill Strength of materials for technicians drotsky solutions Financing Rural Electrification (Legislative Analysis) Its Cold Out There Precious Moments by Enesco Collectors Value Guide 1999 Bottling, kegging, and carbonation Atlantic migrations to the New World Juror number eleven Ch. 10. End-of-life care Journal of international entrepreneurship Conditions in the Coal Mines of Colorado Bitter Creek area of critical environmental concern and Mountain Plover area of critical environmental co Infinite Abelian Groups A Guide to Oracle8 Urchin and the heartstone Gendered dynamics in Latin love poetry A broadcast news manual of style Aaron fisher book silent no more Cold Service (Spenser) Car wash equipment list Life sketches from common paths Diplomatic history of the Caspian Sea How a criminal case works through the courts Entering the summerland The Broadway workout Dom of speech in the united states 8th edition List of the specimens of homopterous insects in the collection of the British museum. The New Managers Tool Kit Fundamentals of chemical engineering thermodynamics si edition Live like you were dying. Introduction : the American Pacific : an errand into Oceania Metres, litres and grams The portable Irish reader The molecular basis of immune cell function Cover letter for marketing manager Silent Notes Taken Taking the road to war Storeys Guide to Raising Meat Goats (Storeys Guides to Raising) The Return of the Moresbys by Henry Slesar