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Simple and Effective Methods for Identifying in Vivo Biomedical Reaction Mechanisms

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Abstract

Background: *Utilizing the separation techniques based on mass spectrometry, molecular spectrometry and various medicinal treatment drugs in the field of biomedicine can help in understanding and applying treatments for a multitude of different disease or diverse types of cancer and even expand upon efficient and reliable diagnosis in clinical settings. However, despite the use of these technologies, interpretation of the measured results is very difficult. Chemical reaction mechanisms, especially nucleophilic substitution reaction mechanism tools can be applied to accurately interpret these measurement results to determine the cause of chronic diseases and develop treatments. Aniline and its derivatives serve as important molecules in biomedicine. Understanding the nucleophilic substitution reaction mechanism of basic molecule as aniline helps to accurately understand the base reactions of DNA in our body cells. How the length of telomeres at the ends of DNA in our body's cells increases or decreases can be understood by applying the reaction mechanism of aniline and its derivatives. Using the nucleophilic substitution reaction mechanism tools of basic molecule likely aniline and their derivatives in the field of biomedicine are available to understand and to apply also treatments for multitude of different diseases like Alzheimer's disease and divers' types of cancer, and to expand on efficient and reliable diagnosis in clinical treatments.*

Summary: *This article deals with the interpretation of reaction mechanisms that can easily understand the pharmacological reaction and cellular response of biomedicine.*

Results: *Molecular nucleophilic substitution reaction mechanism tools of basic molecules likely aniline and their derivatives in the field of biomedicine are available to understand and to apply also treatments for multitude of different diseases like Alzheimer's disease and divers' types of cancer, and to expand on efficient and reliable diagnosis in clinical treatments.*

Conclusions: *By understanding the molecular mechanisms that explain drug reactions and therapeutic effects at the molecular level, it can be used for more precise tracking the causes of cancer and chronic diseases, and the reactions that occur within cells during treatment.*

Keywords: Mass spectrometry, Molecular Spectrometry Cancer, Mechanism, Nucleophilic Substitution, Chronic Disease, Biomedicine, Clinical Treatments.

Introduction

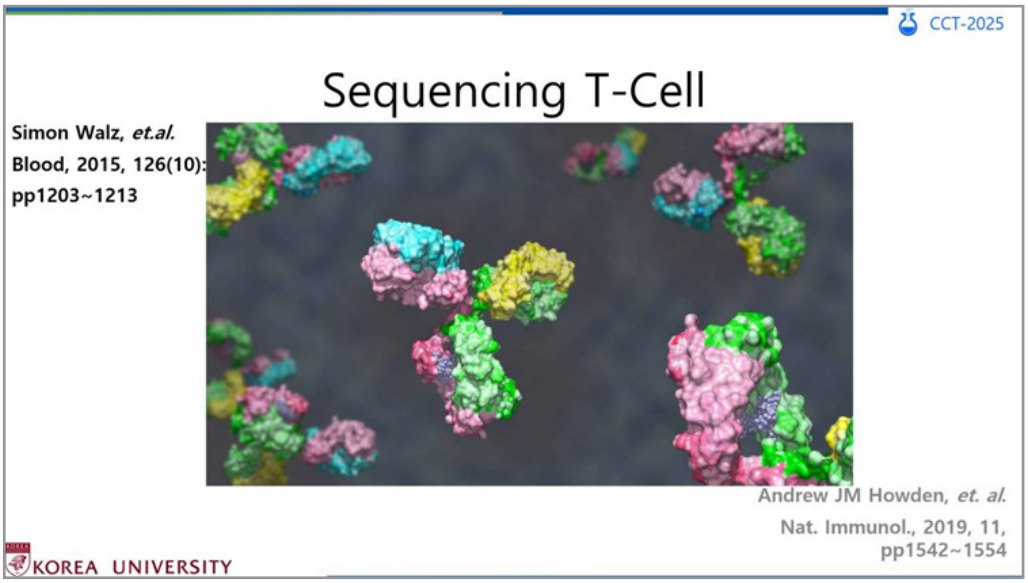
Recently, biomedicine has made a great contribution to the development of the anti- aging field. Biomedical research has revealed that aging mechanisms are deeply linked to the development of cancer and chronic diseases. However, there are still many difficulties in accurately identifying the process by which the human body ages and the causes of chronic diseases. The field of chemical reaction mechanism tools has made a signif-

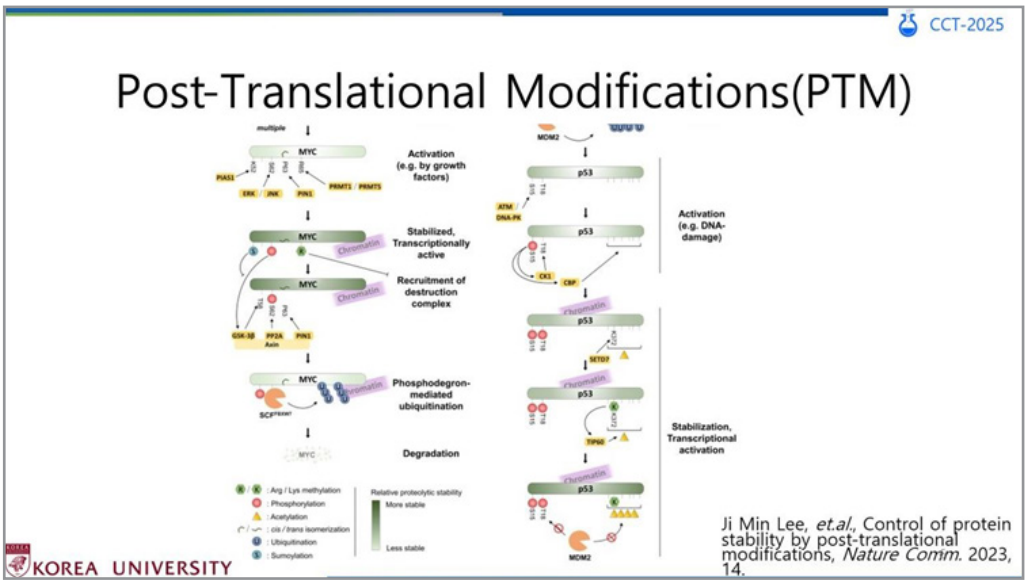
icant contribution to the field of biomedicine. Among the areas of biomedicine, reaction mechanism tools are making a groundbreaking contribution to treating the anti-aging field, which aims to realize the dream of gene scissor therapy and life extension. Understanding of reaction mechanisms is an important role in identifying and resolving the results of measurements of analysis of cellular heterogeneity in gene expression. Although the latest physiological measurements are used to identify the diseases and to provide a lot of measurement data, there are many difficulties in accurately determining the cause of the disease, diagnosing and finally treating it. Recently, new technologies have been used as variant of flow cytometry based on fluorescence, light scattering and separation techniques to sort cells and to confirm the results of measurements. These tools are based on molecular spectroscopy. Laser capture microdissection based on mass spectrometry is helpful to identification that is coupled to a microscope and focused on a tissue. Molecular mass spectrometry is widely applied in RNA sequencing tool based on headspace solid-phase microextraction/gas chromatography-mass spectrometry. Inflammation is one of the major causes of cellular senescence. Inflammatory aging is characterized by increased levels in the proinflammatory factors in the cells. Senescent cells secrete molecules that promote chronic inflammation and organ deterioration, contributing to chronic diseases and aging.

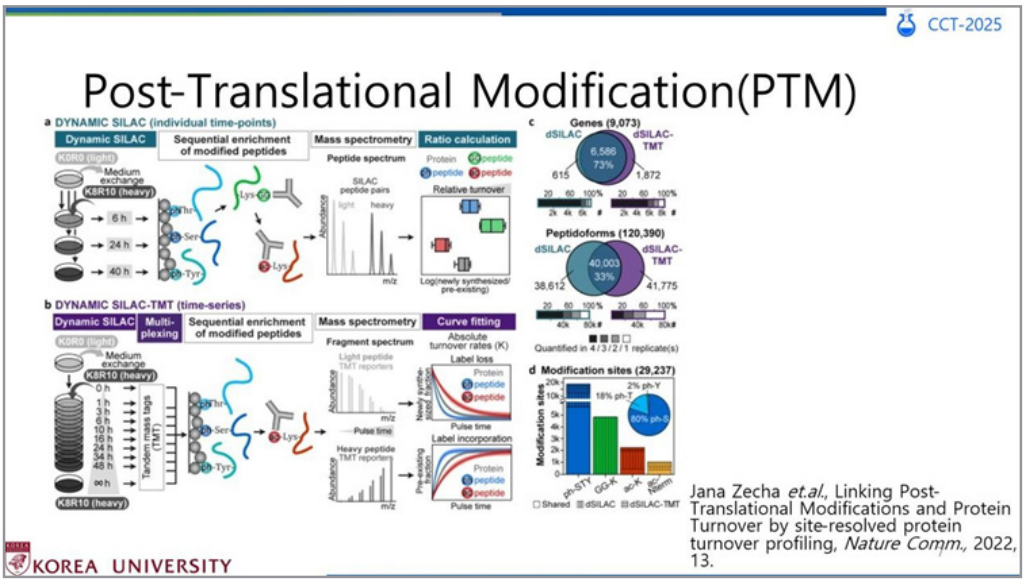
Recent Efforts to Understand Biomedicine at the Molecular Level

The most important challenges facing biomedicine today are completely conquering cancer, understanding chronic inflammation, a precursor to disease, and developing treatments, as well as developing rapid and accurate disease diagnosis methods. Recently, the power of artificial intelligence has been greatly developed in cancer treatment by helping to understand the protein structure of cancer cells in three dimensions. Hospitals are making groundbreaking advances in cancer treatment with boron neutron capture therapy, heavy-particle accelerator therapy, and proton beam therapy. Mass spectrometry is making a significant contribution to identifying the causes of cancer and applying the results to cancer treatment.

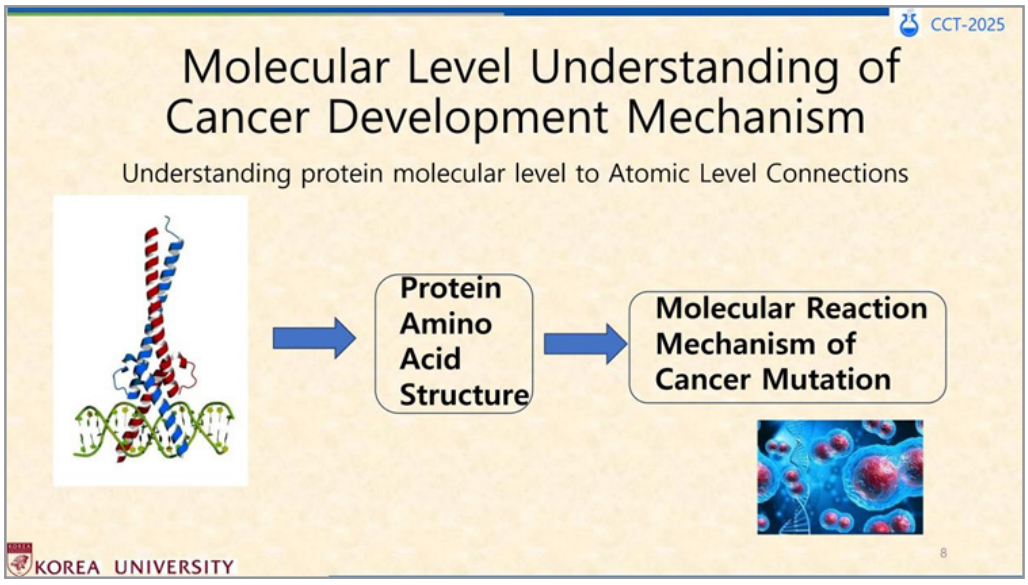
Quantitative mass spectrometry reveals how CD4+ and CD8+ T cells restructure proteomes in response to antigen and mammalian target of rapamycin complex 1 (mTORC1) [1].

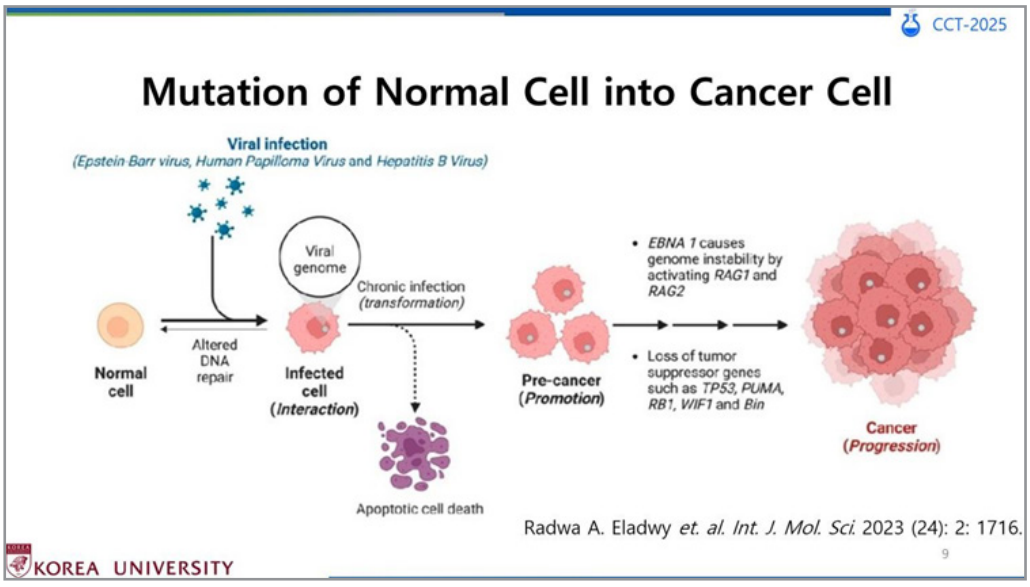






The study of control of protein stability by post-translational modifications (PTMs) has been reported. PTMs possible to explore how protein stability regulates specially, phosphorylation and methylation, can act as signals to either or inhibit protein degradation. PTMs allow us to understand the phenomenon in controlling protein turnover and their impact on cellular process [2]. as activation as DNA- damage, stabilization transcriptional activation.

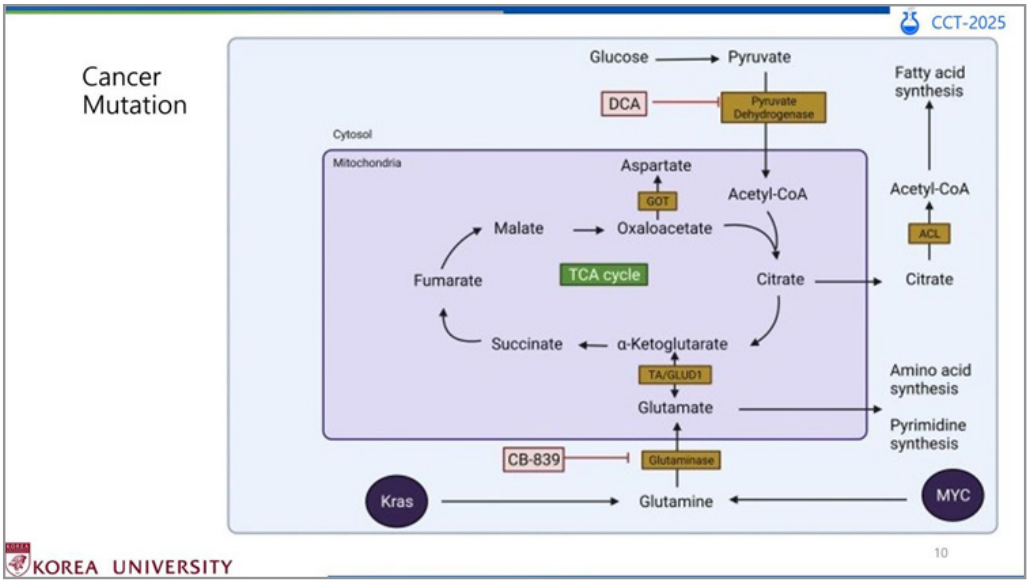




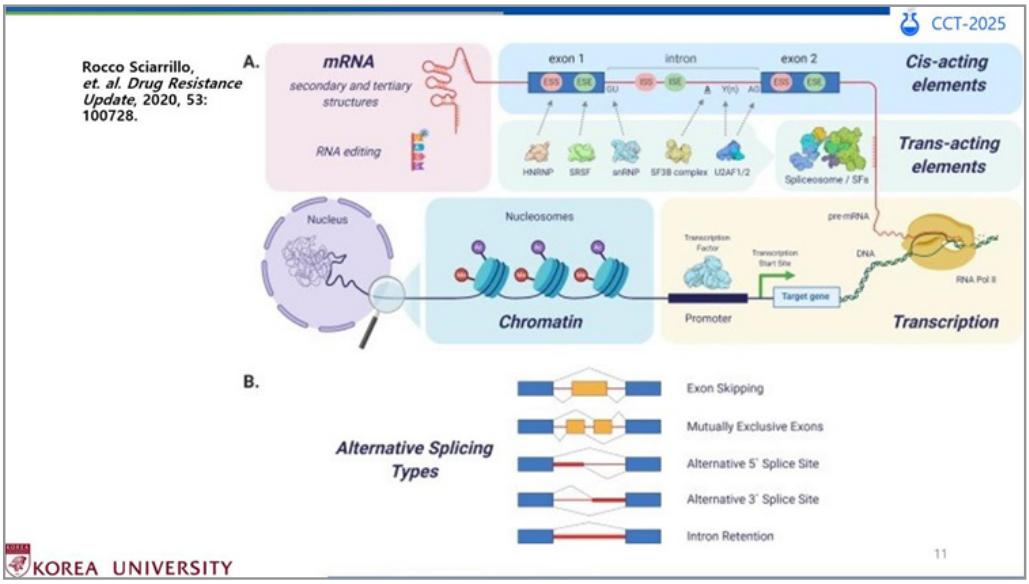
However, proteome-wide measurements of protein turnover have largely ignored the impact of PTMs. To address this gap, the stable isotope labeling and mass spectrometry are used to measure the turnover of many peptidoforms including many kinds of peptides as phosphorylated, acetylated, and ubiquitinated forms [3].

Nowadays PTMs generate an enormous, yet underdetermined, expansion of the produced proteoforms. The concept of proteoforms is highly relevant for understanding top-down perspectives. It has been defined as different molecular forms in which protein products of a single gene can be found, which include changes due to genetic variations, alternatively spliced RNA transcripts, and posttranslational modifications [4]. Proteomic research faces limitations in accurately identifying structural changes. Moreover, efforts to elucidate protein modifications from the molecular level to the three-dimensional structure are still ongoing.

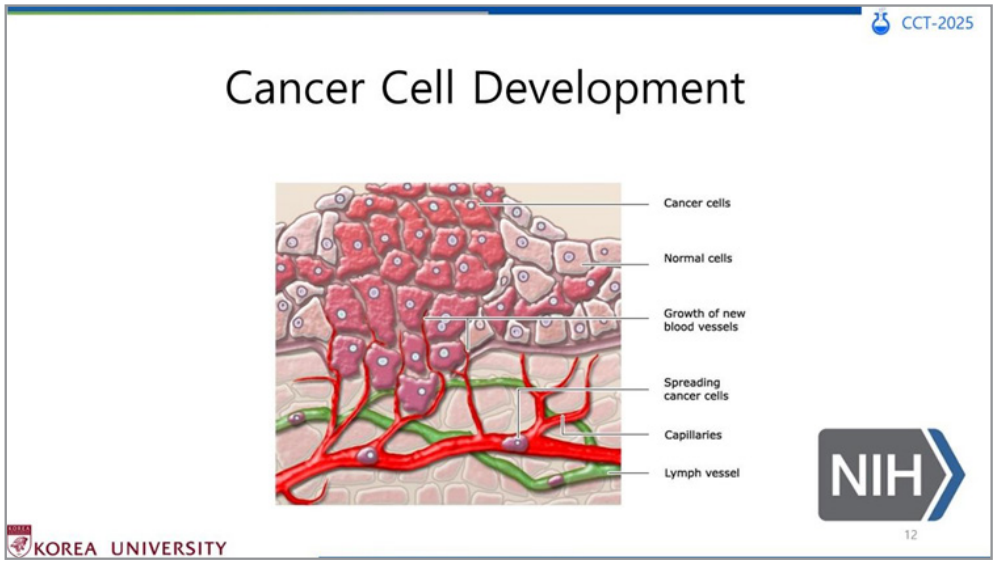
The transformation of normal cells into a cancer cell by virus-mediated carcinogenesis involves initiation, promotion, and progression. An interaction between a carcinogen and the host DNA is initiation, whereas promotion is when cell proliferation occurs. The final step is the spread of the tumor, known as progression [5].



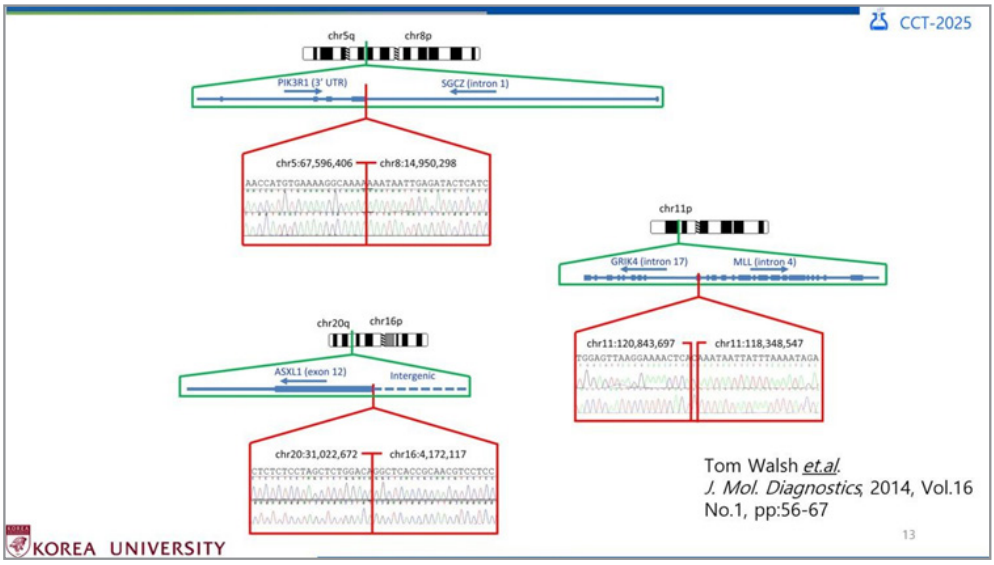
According to these efforts it is known to in cancer, glucose metabolism is often altered, with a key enzyme involved being pyruvate kinase (PK), particularly its pyruvate kinase muscle (PKM) gene and known as the gene encodes for the M2 isoform (PKM2). Mutations in PKM2 are frequently observed in cancer cells and can impact its activity, potentially contributing to the Warburg effect, where cancer cells favor glycolysis even in the presence of oxygen. PK catalyzes the final step of glycolysis, converting phosphoenolpyruvate to pyruvate. The M2 isoform (PKM2) is prevalent in rapidly dividing cells, including cancer cells.



Whole genome/transcriptome sequencing is developed using the high complexity of splicing regulation, which occurs co-transcriptionally and is influenced by chromatin status and mRNA modifications [6]. However, importantly accurate detection of aberrant splicing tools remains a future computational calculation.

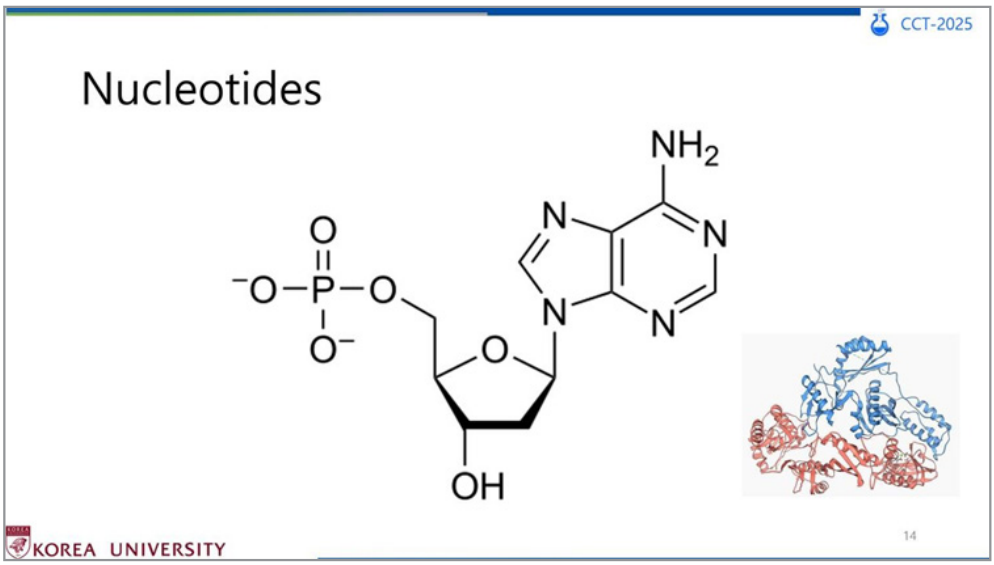


Efforts to elucidate the precise mechanisms by which normal cells transform into cancer cells have made great progress at the genetic level. However, efforts to elucidate the process by which normal cells transform into cancer cells at the molecular level are only just beginning.

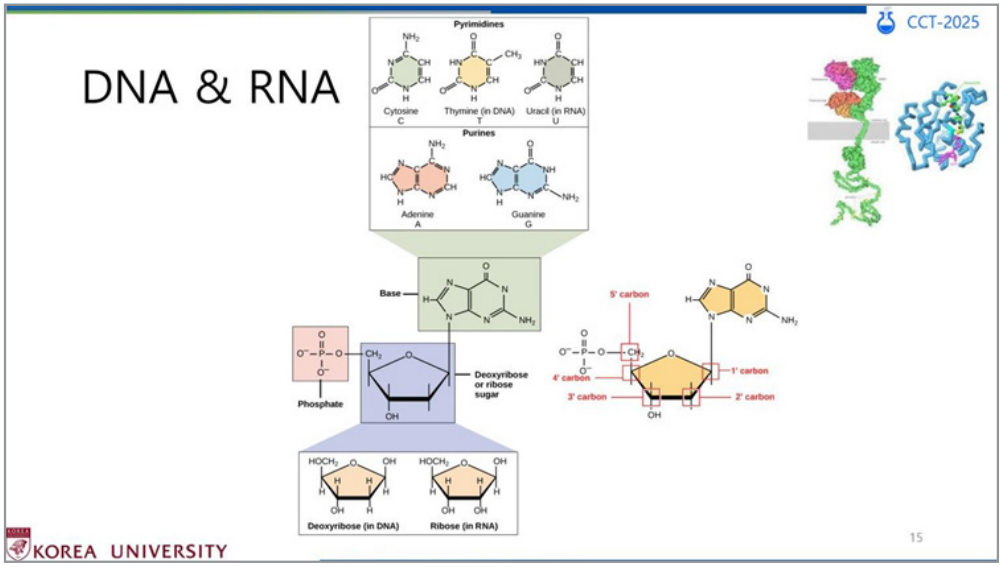


Molecular basis of homozygous familial hypercholesterolemia (HoFH) can explain as defects in the clearance of plasma low-density lipoprotein (LDL), which results in extremely elevated plasma LDL cholesterol (LDL-C) and increased risk of atherosclerosis, coronary heart disease, lipid-lowering therapies are ineffective at lowering plasma cholesterol to safe levels [7].

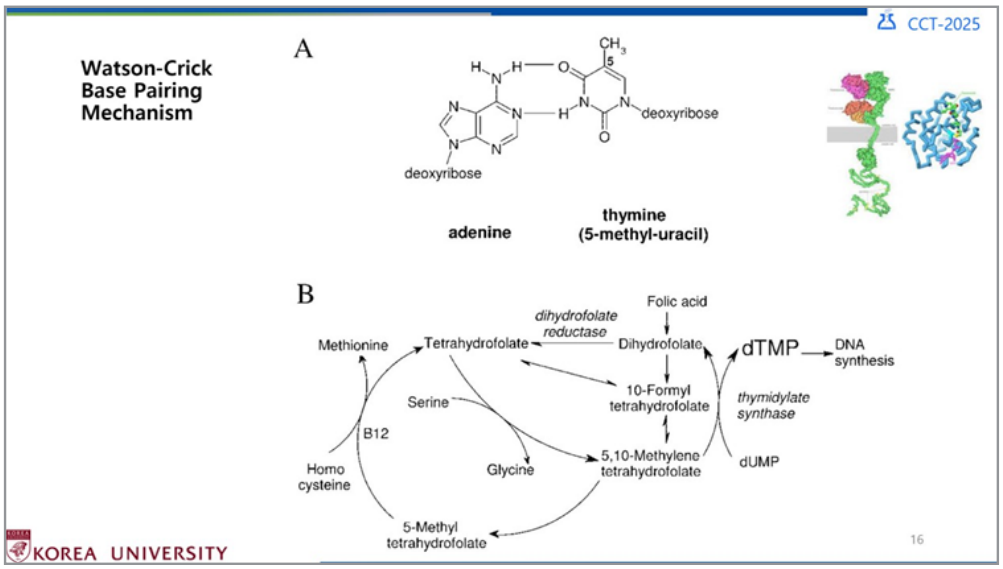
Interpreting Reaction Mechanisms at the Molecular Level in Biomedicine



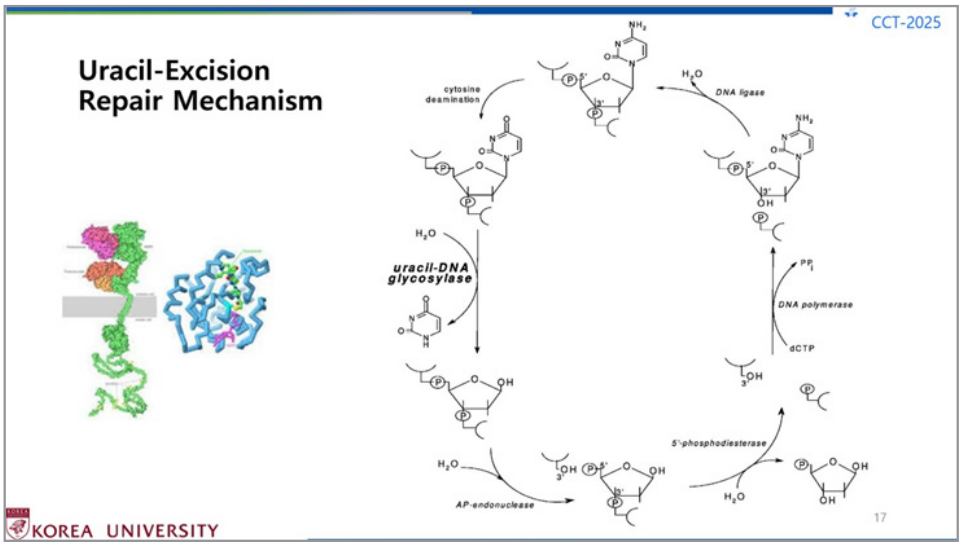
In normal cells, nucleotides are essential to building blocks of DNA and RNA, acting as the fundamental units for genetic information and cellular processes [8]. However, cancer cells exhibit a higher rate of nucleotide synthesis and usage, supporting their rapid and uncontrolled proliferation. This difference in nucleotide metabolism between normal cells and cancer cells can be a target for cancer therapies [9].



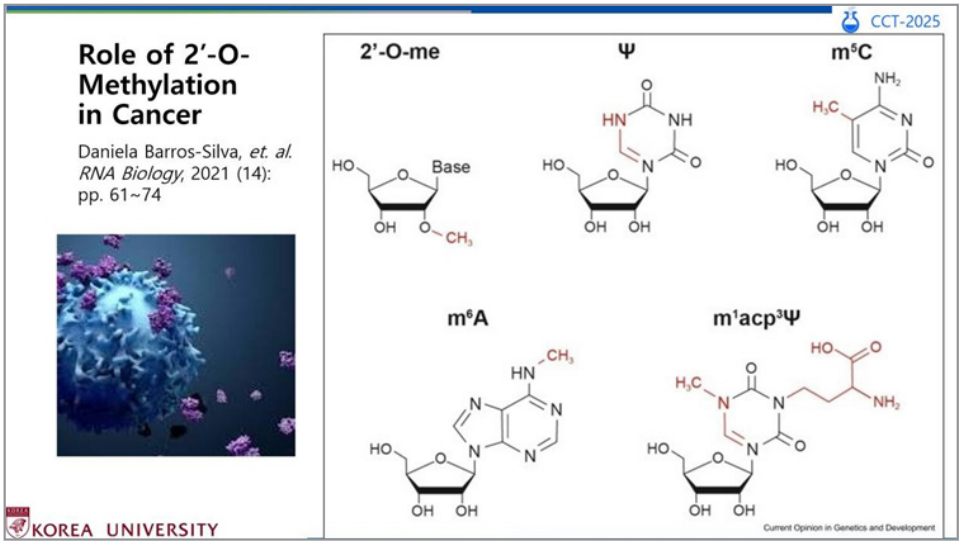
In cancer cells, DNA and RNA differ from their normal cell counterparts in ways that drive uncontrolled growth and division, leading to tumor formation. Mutations in DNA can alter gene expression, causing cells to bypass normal growth controls and evade programmed cell death. These mutations also affect RNA, impacting protein production and potentially promoting metastasis. Cancer cells accumulate mutations in their DNA, affecting genes that regulate cell growth, division, and apoptosis.



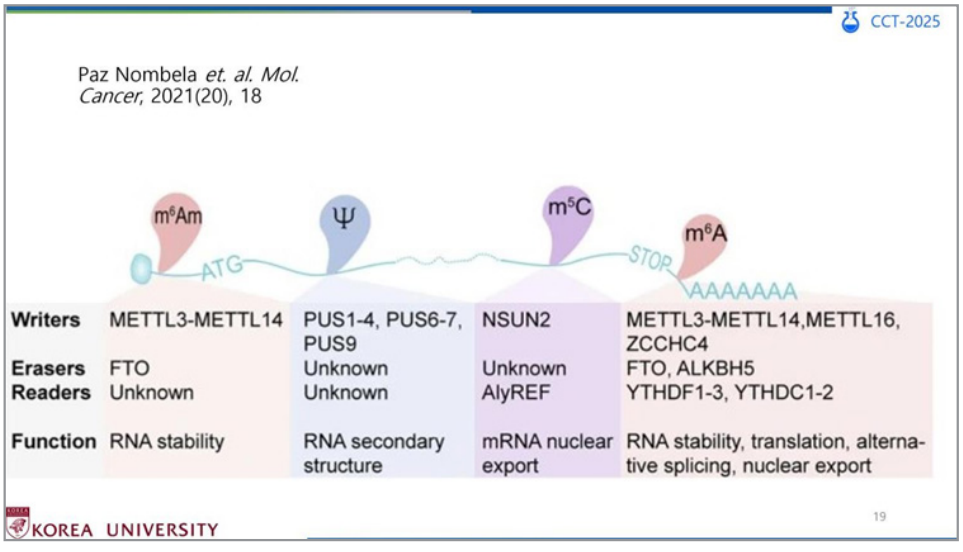
The Watson-Crick base pairing mechanism, which governs how DNA bases pair, that is, A with T, and C with G, is crucial for understanding cancer mutations because errors in this pairing during DNA replication can lead to mutations that contribute to cancer development. These errors, though rare, can accumulate over time and disrupt gene function, potentially triggering uncontrolled cell growth [10].



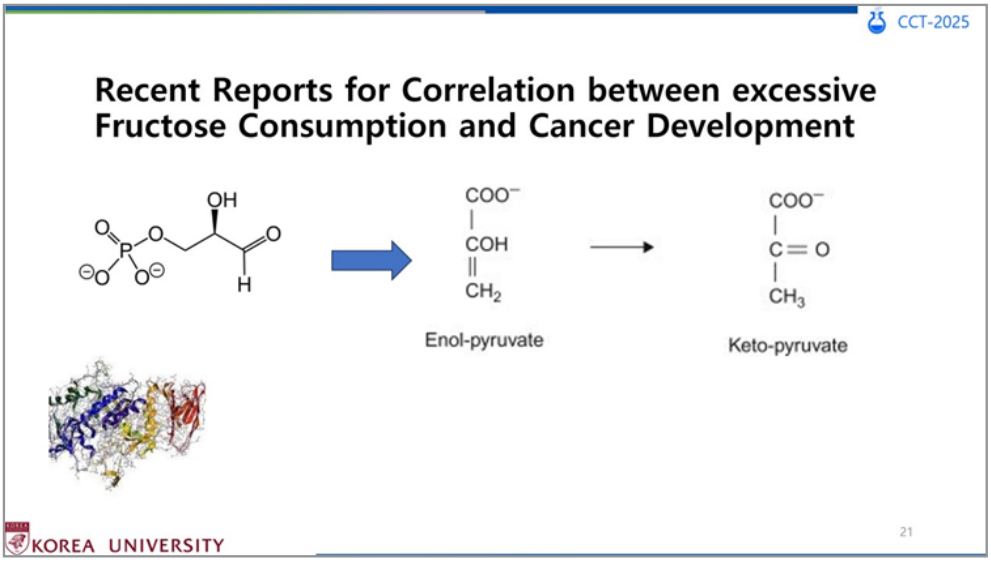
The uracil-excision repair mechanism, primarily base excision repair (BER), is a critical process for removing uracil from DNA. Uracil is a naturally occurring base in RNA, but it can be mistakenly incorporated into DNA during replication or can arise from cytosine deamination. This process involves several steps to remove the uracil and restore the original DNA sequence [11].



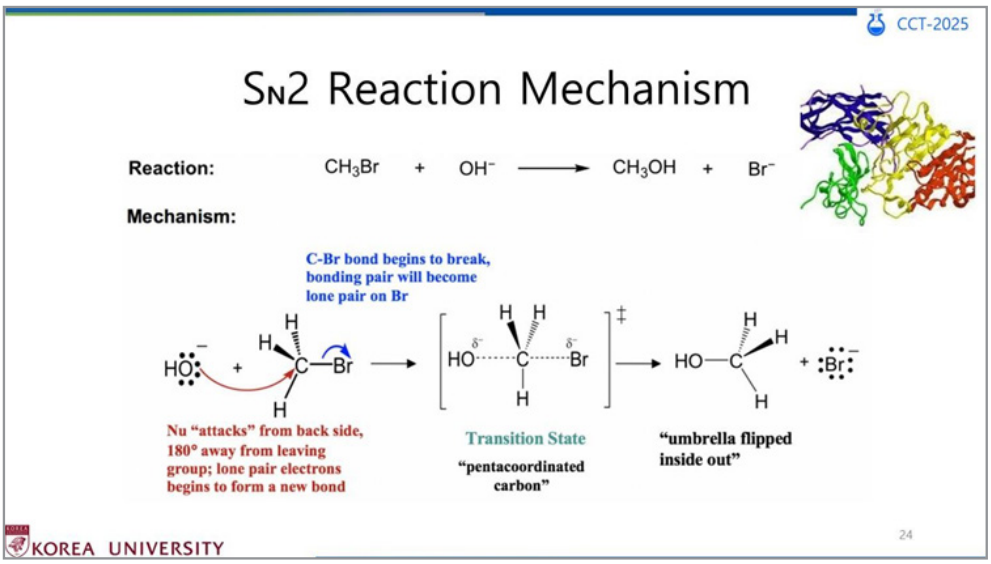
Ribosomes are essential nanomachines responsible for all protein production in cells. Ribosome biogenesis and function are energy costly processes as they are tightly regulated to match cellular needs. In cancer, major pathways that control ribosome biogenesis and functions are often deregulated to ensure cells survival and to accommodate the continuous proliferation of tumor cells. Ribosomal RNAs (rRNAs) are abundantly modified with 2'-O-methylation being one of the most common modifications [12].



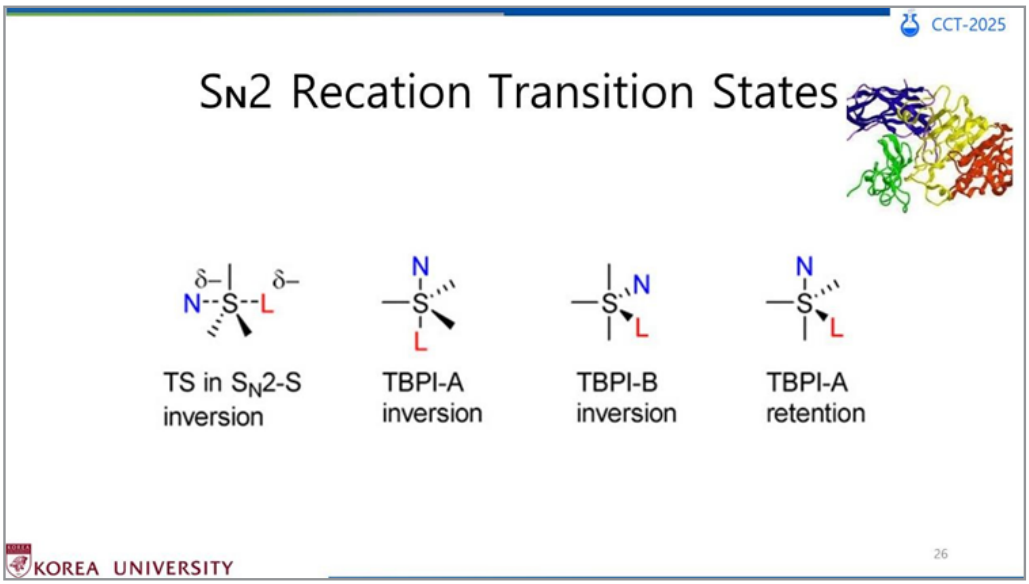
RNA modifications have recently emerged as critical post-transcriptional regulators of gene expression programmed. Significant advances have been made in understanding the functional role of RNA modifications in regulating coding and non-coding RNA processing and function, which in turn thoroughly shape distinct gene expression programmed. They affect diverse biological processes, and the correct deposition of many of these modifications is required for normal development. Alterations of their deposition are implicated in several diseases, including cancer. N6-methyladenosine (m6A) and 5-methylcytosine (m5C) are known two prominent RNA methylation modifications that play significant roles in cancer development, progression, and response to therapy. Epitranscriptomics are known as a field of the study of chemical modifications on RNA molecules and how these modifications influence cancer development, progression, and treatment response. These modifications, like m6A, can affect RNA stability, translation, and interactions, ultimately impacting gene expression and cellular behavior in cancer. Recent advancements in rapidly evolving field of epitranscriptomics have linked the reprogramming of components of epitranscriptomic erasers or readers of the m^6A, m^5C or Ψ to cancer [13, 14]. Despite the achievements of these studies, understanding the process by which normal cells into cancer cells at the molecular level is still a long way off.



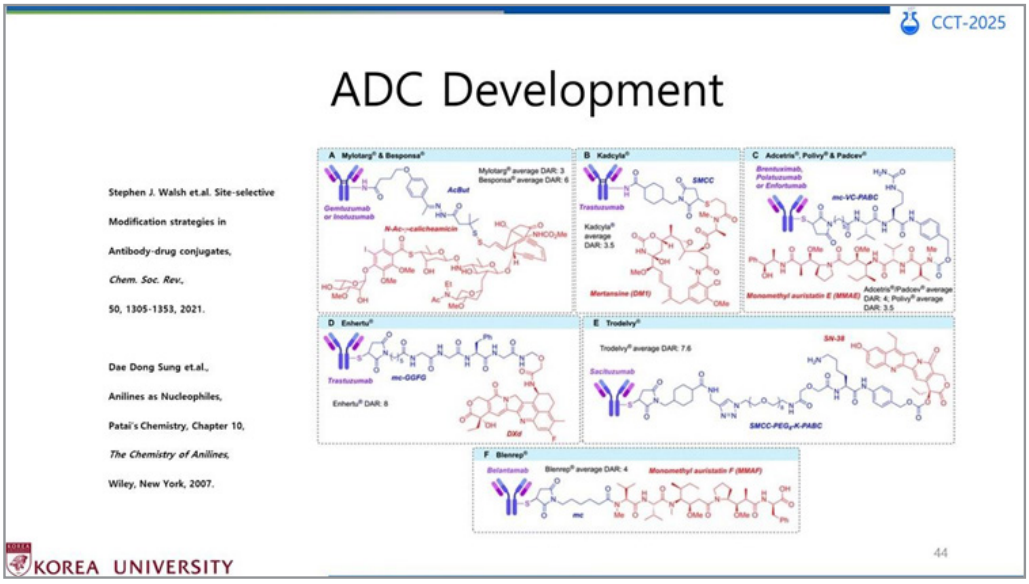
Recent studies have shown that high intake of synthetic fructose can cause pancreatic cancer [15]. Pancreatic cancer cells have a high capacity to utilize fructose and can convert glucose to fructose via the AKR1B1-mediated polyol pathway, in addition to uptake via the fructose transporter GLUT5. Fructose metabolism exacerbates pancreatic cancer proliferation by enhancing glycolysis and accelerating the production of key metabolites that regulate angiogenesis. In pancreatic cancer, the conversion of phosphoenolpyruvate (PEP) to pyruvate kinase M2 (PKM2) is a crucial step in glycolysis and can be influenced by factors like fructose metabolism. In this process, pyruvate is a key product of glycolysis, the process of breaking down glucose for energy. In normal cells, pyruvate can be further processed in mitochondria for energy production of oxidation phosphorylation. In the process, a specific enzyme, PKM2, plays a role in this altered pyruvate metabolism. It exists in active tetrameric and inactive dimeric form. Its activity can be influenced by various factors, including methionine oxidation, which can shift it towards the active tetrameric form and promote respiration and metastasis [16]. Recent studies have shown great success in trying to find the mechanisms of cancer development at the molecular level.



At the molecular level, the mechanism of cancer development can be explained by the nucleophilic substitution reaction mechanism.

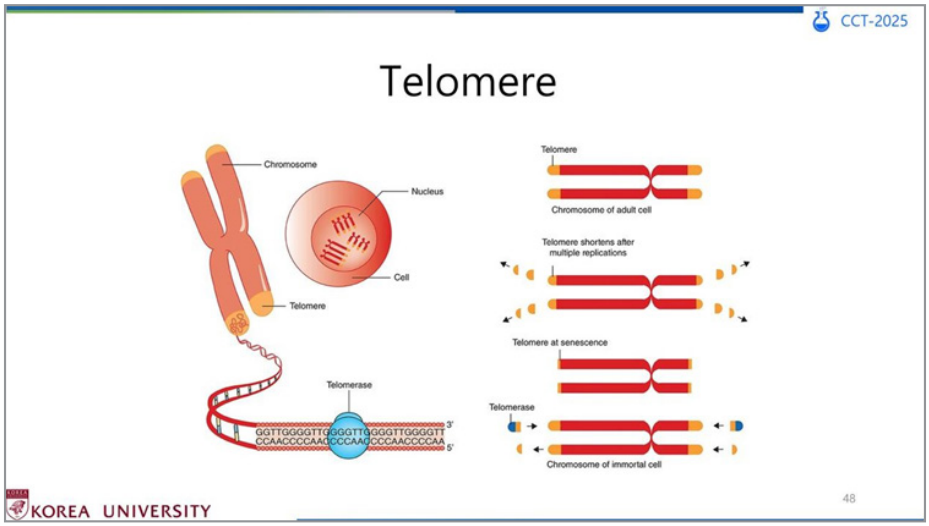


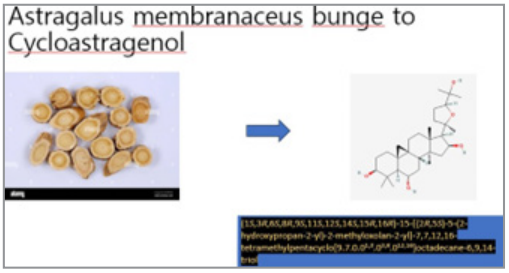
By calculating the energy of the transition state in a nucleophilic substitution reaction, the exact mechanism can be derived from the structure-energy diagram of normal cells when transferred to cancer cells. Through the 3D molecular structure conformation tools, the structure of phospholipids, a component of eukaryotic cell, is being revealed continually. Density functional theory (DFT) is a quantum mechanical modeling method widely used in chemistry and condensed matter physics to study the electronic structure of molecules and solids. However, DFT is typically not used to predict protein structures. Proteins are large biomolecules composed of long chains of amino acids that fold into complex of the three-dimensional structures. The prediction of protein structure is challenging problem in computational biology and biophysics. While DFT can provide valuable insights into the electronic structure and properties of small molecules, it is generally not practical for predicting the three-dimensional structures of large biomolecules like proteins. Although DFT was used as a tool to reveal simple molecular structures, it has been undoubtedly provided the basis for elucidating complex three-dimensional protein structures [17]. Instead, protein structure prediction methods typically rely on the physical organic chemistry that deals with the tools of molecular mechanics fields, molecular dynamics simulations, and other computational techniques specially developed for studying biomolecular systems [18]. These methods of physical organic chemistry and quantum chemistry consider the interactions between atoms in proteins, such as van der Waals forces, electrostatic interactions, and hydrogen bonding, which play a crucial role in determining protein structure. Physical organic chemistry has been connecting DFT to 3D protein structure to find out cancer modification from normal cells.



Cancer treatment has recently been saving many cancer patients with antibody - drug conjugates (ADCs) [19]. ADCs are a type of cancer treatment that combines targeted therapy with chemotherapy. They are designed to deliver a cytotoxic drug directly to cancer cells, minimizing harm to healthy cells. ADCs use monoclonal antibodies (mAbs) that specifically bind to antigens on the surface of cancer cells. In ADCs, this can be explained by the mechanism in which nitrogen or sulfur atoms attack nucleophilic substitution reaction [20]. In ADCs the nitrogen and sulfur atoms in linkers are often involved in forming covalent bonds with the antibody and the payload, respectively, through nucleophilic substitution reaction mechanism [21].

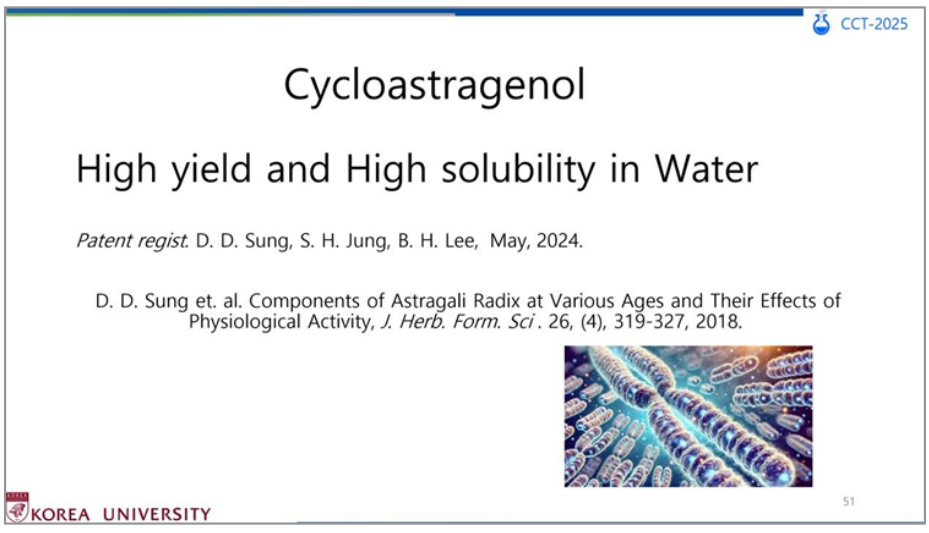
Nitrogen and sulfur atoms are crucial for attaching the linker to both the antibody and the cytotoxic drug, enabling targeted delivery of the drug to cancer cells [22].



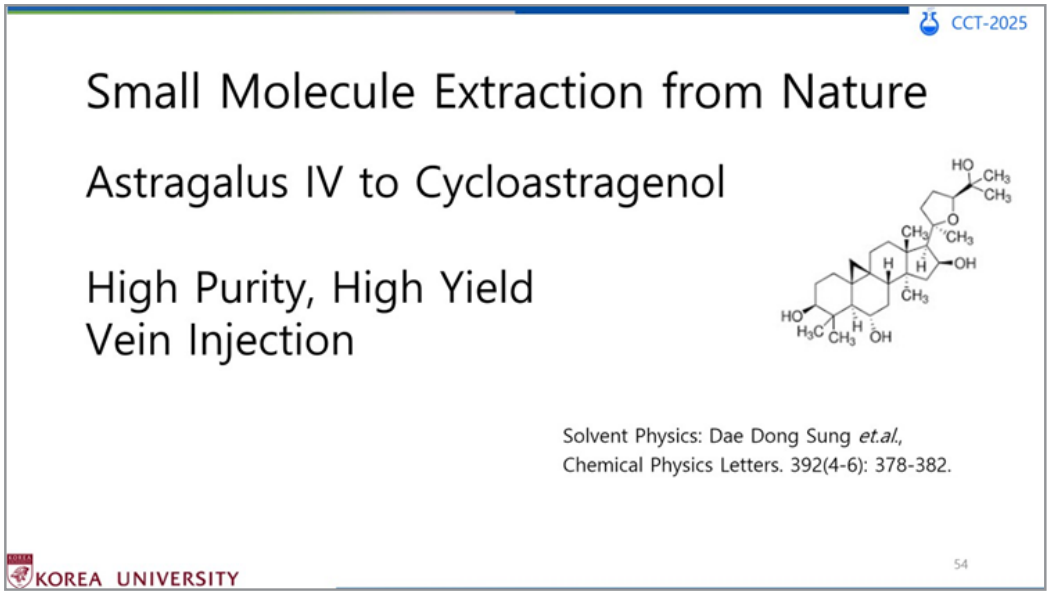


Most eukaryotes stabilize the ends of their linear chromosomes with a telomerase- based system [23]. Telomerase maintains specific repetitive sequences, which protect chromosome ends with the help of telomere-binding proteins [24]. Telomerase adds complementary RNA bases to the end of the DNA strand. Once the end of the lagging strand template is sufficiently elongated, DNA polymerase adds the complementary nucleotides to the ends of the chromosomes; thus, the ends of the chromosomes are replicated. Telomeric dysfunction is caused by shortening, deprotection or damage, and by DNA replication stress, triggers focal accumulation of activated DNA damage response (DDR) factors at telomere dysfunction-induced foci. Shortening of telomeres with each cell division, is caused by the 'end replication problem' and nucleolytic activities, eventually results in loss of protection, DDR activation and appearance of dysfunction-induced foci (TIF), causing cellular senescence or apoptosis. Cancer cells activate telomere maintenance mechanisms to counteract replication-driven telomere shortening. and gain replicative immortality. Most often this is achieved through the re- expression of telomerase, an enzyme that catalyzes the addition of telomeric DNA repeats, but a small part of cancers used to an alternative lengthening of telomeres. The techniques of re-expression of telomerase are developed by fluorescent photochemistry [25].

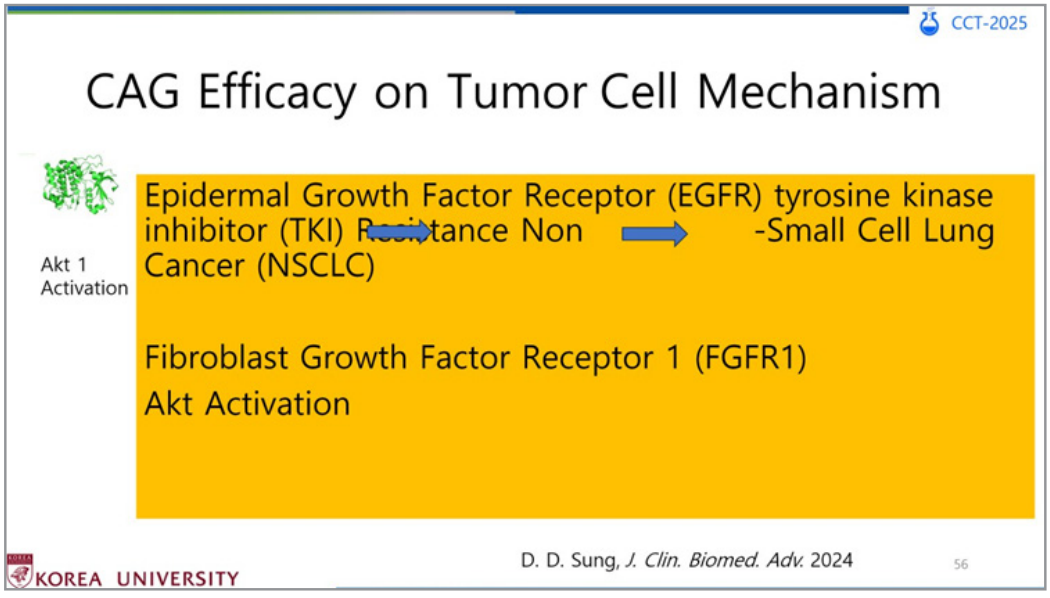
Recently, fluorescent chemists were developing faster and safer analysis techniques by incorporating molecular spectroscopic technology into telomerase enzyme analysis. Through numerous trials and errors, cancer treatment has made remarkable progress. Recently, surgery, radiotherapy and chemotherapy have had many side effects and now only applied to a few cancer patients. Nowadays, immunotherapy and heavy charged particle beam therapy are becoming common. These days, chemists are taking the lead in opening the way to completely treating cancer patients without side effects. Among them, a method to kill cancer cells using immune cells as T-cell, B-cell and natural killer cell within the human body has been developed [26].



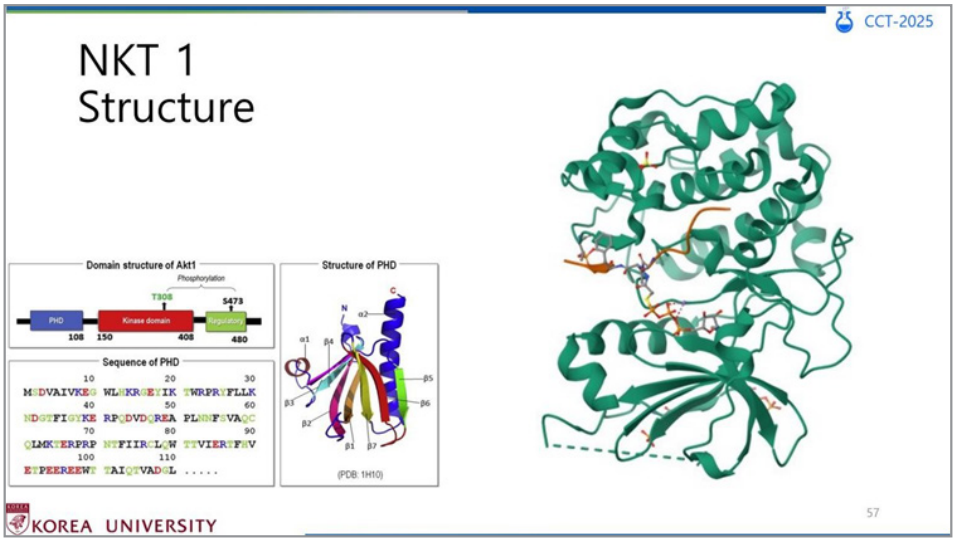
Cycloastragenol (CAG) is a kind of triterpenoid compound derived from the plant Astragalus Membranous [27]. It is known for its potential to activate telomerase, an enzyme that can lengthen telomeres, which are protective caps on the ends of chromosomes. This telomerase activation is believed to play a role in anti-aging and cellular health. CAG affects to be mediated through extracellular signal-regulated kinase (ERK), c-Jun N-terminal kinase (JNK), the pathway of embryonic development, stem cell maintenance, and tissue homostasis regulating gene expression through the stabilization and translocation of beta-catenin to the nucleus with transcription factors (Wnt/β-catenin), activated by phosphadylinositol 3-kinase and then phosphorylates and activates mammalian target of rapamycin (mTOR) (AKT1-mTOR-RPS6KB1) and Janus kinase/signal transducer and activator of transcription (JAK/STA3) mechanisms [28].



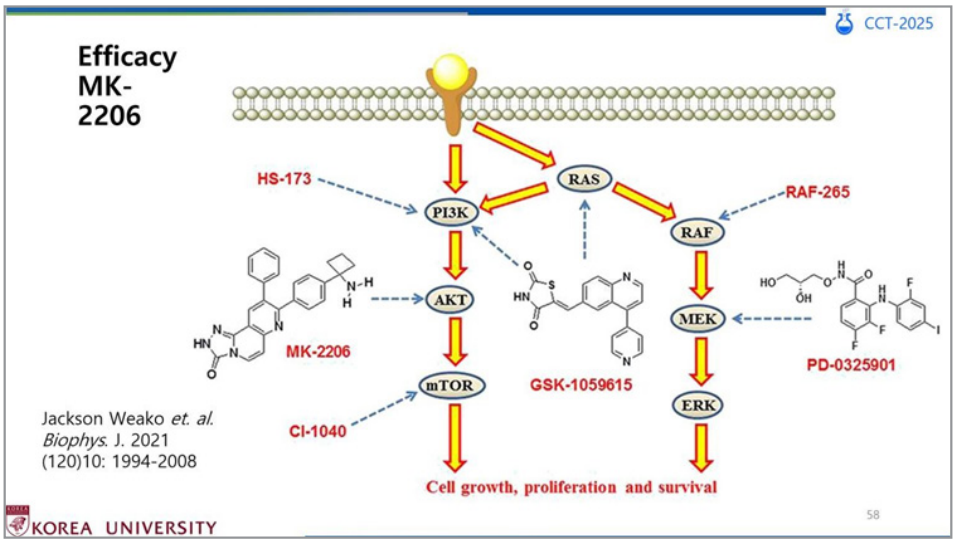
CAG is not very soluble in water and is therefore not well absorbed into human cells. When separating and extracting CAG from Astragalus Membranous, it can be separated and extracted using a nucleophilic substitution mechanism of a hydrophobic solvent [29].



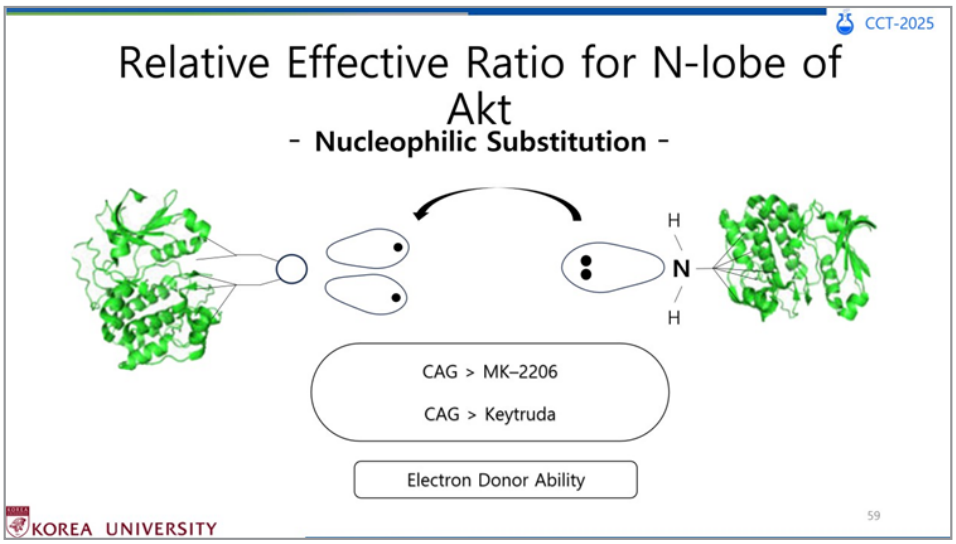
CAG helps treat lung cancer by activating fibroblast growth factor receptor 1 (FGFR1) [25].



NKT 1 cells known as a subset of natural killer T (NKT) cells, a type of immune cells that plays a role in both the innate and adaptive immune responses, particularly in the context of tumor immunity. They are characterized by their ability to recognize lipid antigens presented by the CD1d molecule and by their production of interferon-gamma (IFN-γ) upon activation. In the context of cancer, NKT1 cells can contribute to anti-tumor immunity by directly killing tumor cells or by activating other immune cells like CD8+ T cells and dendric cells [25].



The mechanism of efficacy of MK-2206 is well derived for the process of cell growth, proliferation and survival reactions based on molecular theory. However, the final mechanism by which mTOR acts on growth factors has not been elucidated at the molecular level. The mechanism by which ERK plays a role in cell growth, proliferation, and survival stages has not been elucidated.



Relative effects for ratio of nitrogen atom lobe of Akt is available to elucidate by nucleophilic substitution mechanism [22]. These results show that CAG's cancer treatment effect is greater than that of MK-2206 or Keytruda [25].

Acknowledgments

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Conflict of Interest

No conflict of interest is perceived by the author.

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Relative effects for ratio of nitrogen atom lobe of Akt is available to elucidate by nucleophilic substitution mechanism [22]. These results show that CAG's cancer treatment effect is greater than that of MK-2206 or Keytruda [25].

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Conflict of Interest

No conflict of interest is perceived by the author.

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