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E-POSTERS

Kisok Kim, Asian J Biomed Pharmaceut Sci 2018, Volume 8 | DOI: 10.4066/2249-622X-C3-009

CHARACTERIZATION OF PHENOLIC ACIDS AND FLAVONOIDS IN ETHYL ACETATE FRACTION OF *ASTER GLEHNI*

Kisok Kim
Keimyung University, Republic of Korea

Aster glehni is widely distributed in Korea. However, detailed information on phenolic compounds of this plant are lacking. We identified phenolic acids and flavonoids in an ethyl acetate extract of *Aster glehni*. Phytochemicals were extracted from leaves into methanol, and an ethyl acetate extract was subsequently prepared. Phenolic acids and flavonoids were identified via gas chromatography-mass spectrometry (GC-MS) and liquid chromatography-tandem mass spectrometry (LC-MS/MS), respectively. Caffeic, ρ-coumaric acid, protocatechuic acid, 4-hydroxybenzoic acid, and salicylic acid were the major phenolic acids, and the levels of astragalin, hyperoside, kaempferol, and rutin were the highest among the 9 identified flavonoids. These results suggest that the ethyl acetate fraction of *Aster glehni* leaves may exhibit significant antioxidant and health-promoting activity, which is attributable to the high levels of phenolic acids and flavonoids.

BIOGRAPHY

Kisok Kim has completed his PhD from Seoul National University, Korea. He is a research scholar of Keimyung University, Korea. He has over 50 publications in reputed journals.

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ASSOCIATION BETWEEN DEPRESSION AND HEALTH-RELATED QUALITY OF LIFE IN POST-MENOPAUSAL WOMEN

Hyejin Park
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The purpose of present study is to estimate the association between depression and health-related quality of life (HRQoL) in post-menopausal women. Participants (n=3,860) were selected from Korea National Health and Nutrition Examination Survey [KNHANES] 2013-2015. Socio-demographic characteristics, medical history of depression, and EQ-5D were gathered from the KNHANES dataset. The results showed that demographic variables, including age, education level, and income were important factors associated with HRQoL. In this study, depression was an important factor affecting HRQoL in post -menopausal women. The adjusted odds ratio for HRQoL in participants with depression was 5.52 [(95% confidence interval (CI)=4.04-7.55, p<0.001)] in anxiety/depression, 3.86 (95% CI=2.78-5.36, p<0.001) in usual activities, and 2.52 (95% CI=1.68-3.78, p<0.001) in selfcare. These findings suggest that there is a strong relationship between depression and HRQoL and preventing the onset or deterioration of depression may significantly improve the quality of life for post-menopausal women.

BIOGRAPHY

Hyejin Park has completed her PhD from Kyungpook National University, Korea. She has conducted researches at Daegu Catholic University and her research interests span both public health and epidemiology. Much of her work has been on improving the understanding of diseases relating to women and elderly, mainly through the application of epidemiological approaches.

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LIFE STYLE AND ENVIRONMENTAL FACTORS INFLUENCE THE IQ IN CHILDREN AND ADOLESCENTS- A STUDY IN MALAYSIA

Swamy KB
Assam Agricultural University, India

Intelligence quotient (IQ) is widely used to assess different aspects of mental ability. Development in mental ability initiates from conception and continues through adulthood. Various environmental factors affect IQ. The aim of this study was to assess the correlation between IQ and environmental characteristics on cranial capacity in children and adolescents in Malaysia. This cross-sectional study was performed on primary and secondary school students in Kuala Terengganu, Malaysia. Students, who were aged between 6 to 16 years and did not have any mental or physical disabilities, participated in this study. Measurements including weight, height, body mass index and cephalometry were performed for each subject. The Wechsler Abbreviated Scale of Intelligence-second edition (WASI-II) questionnaire was used for each subject to evaluate the subtests of IQ. A total of 419 subjects with the mean age of 12.51±2.82 years had participated in this study. Boys were taller ($p=0.04$), had higher IQ ($p=0.01$) and cranial capacity ($p<0.001$) as well as block design score ($p=0.02$) when compared with girls. There was a significant mean effect for age ($p=0.03$), gender ($p=0.04$), paternal education ($p=0.04$), family income and block design ($p=0.03$) on cranial capacity. This study revealed different patterns of brain growth, function and IQ amongst male and female subjects as well as defining the environmental factors that can affect cranial capacity and that the IQ and cranial capacity may be improved by tuning up the lifestyles and economic conditions of the families in developing countries.

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BIO-ANALYTICAL METHODS FOR QUANTITATIVE DETERMINATION (BIO-EQUIVALENCE AND BIO-AVAILABILITY) OF DRUG PRESENT IN THE BLOOD MATRIX

Aashna Lamba and Swastika Mishra
Amity University, India

Bio-analytical methods utilized for the quantitative determination of drugs and their metabolite in biological matrix such as, plasma, urine, saliva and serum in order to find their significant role in evaluation of interpretation of bioavailability and bio-equivalence for Pharmacokinetic data. The evaluations for linearity, precisions, accuracy and sensitivity were performed on three batches of spiked plasma samples. Each batch of spiked plasma sample included one complete set of calibration standards (blank, blank plus internal standard etc). Each different blank matrix batches were screened for interference at the retention time (RT). Bulk spiking of the samples were prepared by several dilution with analyte free plasma to obtain eight different concentration level. The closeness of the mean test results obtained by method to the true value (concentration) of the analyte showed the precision of the analytical method. Accuracy was determined by replicate analysis of samples. Large set of low, middle and high quality control (QC) samples were processed and analyzed against a single calibration curve. The following pharmacokinetic parameters were calculated for analyte using software- AUC0-t, AUC0-24, AUC-∞, AUC%, Cmax, Tmax and T1/2.

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FLUORESCENT AND T1 MRI ACTIVE MULTILAYER NANOPARTICLE FOR IMAGING AND TARGETING CELLULAR DELIVERY

Oara Neumann
Rice University, USA

Multifunctional plasmonic nanostructures have enormous potential in the treatment of solid tumors; however, tracking particles with drug cargo and triggering the release of the cargo in mapped tumors is still impossible. To overcome this challenge we have developed an MRI and fluorescent active nanostructure nanomatryoshka. This new nanostructure with IR plasmonic signatures is composed of a 50 nm Au core surrounded by dye molecules and Gd(III)-DOTA chelate doped SiO2 inner-shell and an outer Au shell. The experimental results demonstrates an enhanced T1 relaxation (r_1~24 $mM^{-1}s^{-1}$ at 4.7 T) compared to the clinical Gd(III)-DOTA chelating agents (r_1~4 mM^{-1} s^{-1}). Further, this design preserves the fluorescence signal (65%) after 24 hours of exposure, leading to enahanced fluorescence photostability (23x). This dual-imaging functionality nanosystem increases MRI sensitivity by concentrating Gd(III) ions into the Gd-NMs, reduces the potential toxicity of Gd(III) ions and dye molecules by preventing their release *in vivo* through the outer Au shell protection, and the terminal gold layer surface can then be functionalized to increase cellular uptake, circulation time, or thermal drug-release properties.

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DIRECT EVIDENCE OF VIRAL INFECTION AND MITOCHONDRIAL ALTERATIONS IN THE BRAIN OF FETUSES AT HIGH RISK FOR SCHIZOPHRENIA

Segundo Mesa Castillo
Psychiatric Hospital of Havana, Cuba

There is increasing evidences that favor the prenatal beginning of schizophrenia. These evidences point towards intra-uterine environmental factors that act specifically during the second pregnancy trimester producing a direct damage of the brain of the fetus. The current available technology doesn't allow observing what is happening at cellular level since the human brain is not exposed to a direct analysis in that stage of the life in subjects at high risk of developing schizophrenia. In 1977, we began a direct electron microscopic research of the brain of fetuses at high risk from schizophrenic mothers in order to finding differences at cellular level in relation to controls. In these studies we have observed within the nuclei of neurons the presence of complete and incomplete viral particles that reacted in positive form with antibodies to herpes simplex hominis type I [HSV1] virus, and mitochondria alterations. The importance of these findings can have practical applications in the prevention of the illness keeping in mind its direct relation to the aetiology and physiopathology of schizophrenia. A study of the gametes or the amniotic fluid cells in women at risk of having a schizophrenic offspring is considered. Of being observed the same alterations that those observed previously in the cells of the brain of the studied foetuses, it would intend to these women in risk of having a schizophrenia descendant, previous information of the results, the voluntary medical interruption of the pregnancy or an early anti HSV1 viral treatment as preventive measure of the later development of the illness.

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MOLECULAR PROFILING AND PERSONALIZED MEDICINE OF NON-SMALL CELL LUNG CANCER AND COLORECTAL CANCER

Dongfeng Tan
University of Texas, USA

Personalized medicine, in concert with targeted oncologic therapy, has become one of the most active, rapidly advancing, and clinically challenging pursuits in cancer treatment. A major concern for molecular geneticists and clinicians must be to focus upon prioritizing those issues that are most important for research and targeted management in these most prolific days of cancer medicine. In no area of medicine is this more apparent than in cancer medicine, where arrays of specific genetic alterations have been used to manage various types of malignancies. The discoveries that form our understanding of cancer have substantially accelerated over the past decade. These emerging findings have significantly affected the traditional practice of oncology and have resulted in a subspecialized multidisciplinary approach to patient care that incorporates personalized therapies such as targeted molecular therapy, prognosis, risk assessment, and prevention, all of which are primarily based on molecular diagnostics and imaging. This presentation, using non-small cell lung cancer and colorectal cancer as models, updates readers on recently acquired knowledge of molecular pathology and emphasizes new uses for that knowledge in the changing landscape of specialized multidisciplinary care and personalized medicine. Novel therapeutic agents against specific genetic, molecular, and antigenic targets are discussed, as is the process for deciding whether to use these agents. Furthermore, recent developments in targeting cancer stem cell to avoid drug resistance, recurrence and metastasis are to be discussed.

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HISTOPATHOLOGY – FROM SUPPORTIVE TO DOMINANT TOOL IN PRECLINICAL EFFICACY STUDIES

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Patho-Logica, Israel

The histopathological evaluation in preclinical efficacy studies is often biased due to unsuitable methods, lack of standardization and use of qualitative observations. A comparison between studies is difficult because of the diversity of assays used to assess a similar tissue and injury. In addition, the need for a specifically trained expert to analyze the histological data also leads to the lesser use of histology in the R&D of drug development. The aim of this presentation is to demonstrate the contribution of quantitative measures and advanced image analysis tools to seek for an unbiased histopathological evaluation. By choosing the most relevant parameters, that best suit the scientific questions being addressed, investigators may overcome the risk of incorrect interpretation. Examples of a quantitative assessment of multiple histological features for various injuries will be shown, indicating the advantages of using a computerized image analysis system for densitometry and for morphometric analysis. The latter is critical for the assessment of the extent of tissue injury in efficacy studies in experimental animal models. Attention will be drawn to lung tissue and free-floating brain sections. Quality assurance measures support the histopathological analysis, contributing to the reduction of errors and to the ability to detect subtle differences between treatment groups. In summary, the scientific impact of histopathology in preclinical efficacy studies at present, is increasing and becoming dominant due to the greater use of advanced methodology and quantitative analysis.

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BREAST CANCER AND BMI: ROLE OF L-CARNITINE IN PREDICTION OF ANSWER TO TREATMENT AND OUTCOME OF TUMOR IN PATIENTS WITH OBESITY

Hojouj M I M
Dnipropetrovsk Medical Academy, Ukraine

Increasing the effectiveness of antitumor therapy in breast cancer patients who take L-carnitine during preoperative systemic antitumor therapy compared with patients receiving standard neoadjuvant systemic antitumor therapy served as a prerequisite for studying possi-ble antitumor mechanisms of L-carnitine. The positive effect of L-carnitine is due to the trans-fer of palm-n-fatty acid through the inner membrane into the mitochondrial matrix, which contributes to the formation of a significant number of ATP molecules. It has also been shown that L-carnitine can have a double protective effect, enhancing the energy dynamics of the cell and inhibiting the hyperexcitability of the cell membrane, making it an ideal tool for the prevention and treatment of complications of antitumor therapy and concomitant metabolic disorders. This work summarizes the results of epidemiological and clinical studies on the use of L-carnitine in the treatment of breast cancer.

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STRUCTURE-BASED DESIGN FOR BINDING PEPTIDES IN ANTI-CANCER THERAPY

John Yu
Chang Gung University, Taiwan

The conventional anticancer therapeutics usually lack cancer specificity, leading to damage of normal tissues that patients find hard to tolerate. Ideally, anticancer therapeutics carrying payloads of drugs equipped with cancer targeting peptides can act like "guided missiles" with the capacity of targeted delivery toward many types of cancers. Peptides are amenable for conjugation to nano drugs for functionalization, thereby improving drug delivery and cellular uptake in cancer-targeting therapies. Peptide drugs are often more difficult to design through molecular docking and *in silico* analysis than small molecules, because peptide structures are more flexible, possess intricate molecular conformations, and undergo complex interactions. In this report, the development and application of strategies for structure-based design of cancer-targeting peptides against GRP78 are discussed. The author will also cover topics related to peptide pharmacokinetics and targeting delivery, including molecular docking studies, features that provide advantages for *in vivo* use, and properties that influence the cancer-targeting ability. Some advanced technologies and special peptides that can overcome the pharmacokinetic challenges have also been included.

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PRECISION SYSTEMS MEDICINE IN UROLOGICAL TUMORS – MOLECULAR PROFILING AND FUNCTIONAL TESTING

Khalid Saeed
University of Helsinki, Finland

Background: Most precision cancer medicine efforts are based on the identification of oncogenic driver mutations by genome sequencing. We believe and have emerging evidence that this will miss therapeutic opportunities and additional technologies, such as cell -based functional testing should be included. Pioneering studies in leukemia indicate the value of ex vivo drug testing to identify novel, clinically actionable therapeutic opportunities.

Methods: Using conditional re-programming technology, we established patient-derived cells (PDCs) from castration-resistant prostate cancer (CRPC) and renal cell cancer (RCC) to pilot precision systems medicine in solid tumors. The PDCs were compared with primary tumor tissue by genomic profiling and then subjected to drug sensitivity testing with >306 approved and investigational oncology drugs.

Results: Here, we generated both benign and malignant PDCs from prostate tissue, including six benign PDCs that were androgen receptor (AR) -negative, basal/transit-amplifying phenotype, but could re-express AR in 3D-culture. The PDCs from a CRPC patient displayed multiple CNAs, some of which were shared with the parental tumor. The cancer-selective drug profile for these PDCs showed sensitivity to taxanes, navitoclax, bexarotene, tretinoin, oxaliplatin and mepacrine. RCC displays extensive intra-tumor heterogeneity and clonal evolution. There is, however, very little information on how much this impacts drug sensitivities. Therefore, we generated several PDCs from each RCC patient across multiple tumor regions. We verified their clonal relationship with the uncultured tumor tissue by NGS and performed drug sensitivity profiling. The PDCs retained CNAs and driver mutations in e.g., VHL, PBRM1, PIK3C2A, KMD5C, TSC2 genes present in the original tumor tissue. Drug testing with 461 oncology drugs identified shared vulnerability among the multiple PDCs to pazopanib and temsirolimus that inhibit well-established renal cancer pathways VEGFR/PDGFR/FGFR and mTOR. Importantly, however, the individual PDC from different regions in one patient also showed distinct drug response profiles, confirming that genomic heterogeneity leads to variability in drug responses.

Conclusions: Our aim is to generate molecular profiles and drug testing data using representative PDCs from each patient to help clinicians in treatment decision and to facilitate the early selection of the best drug candidates for clinical development. We believe this approach will help to personalize treatment, prioritize drugs for clinical testing, provide for intelligent selection of drug combinations and improve treatment outcomes.

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CMC STRATEGIES TO EFFECTIVELY MANAGE CMC DATA CHALLENGES AND ENSURE REGULATORY COMPLIANCE IN JAPAN

Seema Singh
Impute Inc., Japan

The amount of Chemistry, manufacturing, and controls (CMC) information needed varies according to formulation type, drug category and jurisdictions. And Japanese regulatory landscape is often perceived as having complicated processes, stringent drug approval standards, language and culture barrier, which are considered by many to be the most challenging in the world. It's very important to understand Japan specific regulatory requirements and preemptively identify CMC data challenges to enable accelerated drug development and approval in Japan. The propose is to identify the priority measures and controls that companies should have in place to build quality into procedures for compiling flawless regulatory submissions and to reduce review time by minimizing regulatory queries, appropriately deal with CMC data challenges. Scientific, robust and adaptive CMC development strategy is essential when dealing with PMDA-interactions, submission conformance or compliance and overall probability of success of the Japan-NDA. Key considerations for formulating and implementing a successful regulatory strategy are: Understanding of marketing authorization application process, key stages, PMDA review and expectations; CMC requirements in Japan focusing on rationalization for setting scientifically sound specifications, stability program, correct interpretation of stability data and shelf life claim as specification and stability are of immense importance in the development of safe and efficacious formulations; CMC review and GMP compliance and; how to utilize prior explicit and tacit knowledge on CMC requirements from successful approvals or PMDA quality consultations meetings, tactical planning, alternative approaches to justify data lacking in CMC package and to ensure the requirements are met to PMDA approval process.

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THE ACCESS TO PRODUCE COMPATIBLE VIRAL VACCINES FOR INDIVIDUALITY

Tirasak Pasharawipas
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There is a question why viral vaccines cannot be effective for everybody. This is a question that we need to revise our knowledge and manipulate in the right direction for the viral vaccine production. To prevent a viral infection, a body must produce a protective antibody to prevent the viral particle to attach the viral receptor on a target cell. Theoretically, adaptive immunity needs induction not only by an antigen but also our cellular molecule called major histocompatibility complex (MHC) to form a complex molecule with its appropriate epitope to activate a specific receptor of T cell. There are two classes of MHC molecules called class I and class II. MHC class I is required for inducing cytotoxic T cell while MHC class II is for helper T cell. Helper T cell plays a key role to induce an effective stage of acquired immunity including a specific protective antibody. To produce the viral-specific antibody, MHC class II plays a key role to induce helper T cell and then B cell to synthesize a specific antibody. Since the MHC gene alleles are highly polymorphic so the possibility that individuals have the same gene alleles might be one in a million which, mostly, can be found in those who are an identical twin. Accordingly, a subunit viral vaccine, which contains a limit number of epitopes, would reduce a capacity of an antigen presenting cell, such as a dendritic cell, to process some epitopes to induce the helper T cell clones. Subsequently, in some people, the corresponding B cell clones cannot synthesize the specific antibody to neutralize the infectious viral particle. Accordingly, this presentation will present the novel approach to develop the viral vaccine for everybody.

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TOWARD-ANTI-AGING AND LONG-LIFE SYNTHESIS OF ANTI-AGING REAGENTS SULFO DISACCHARIDES CO-WORKING WITH KLOTHO (ANTI-AGING GENE)

Showchiro Ozaki
Brain Science Institute, Japan

Nabeshima found Klotho (anti-aging gene) and sulfo disaccharide, co-working with Klotho. Ozaki synthesized several disaccharides and found the structure and the mechanism how these compounds are working. The disaccharide has glucosamine structures and similar structure with hyaluronic acids and chondroitin. Klotho makes disaccharides (glucronosyll (1-3) (N-acetyl glucosamine. From glucosamine and glucuronic acid and co-works on site with produced disaccharide and gives stable Ca homeostasis and consequent health, anti-aging and long life. Glucosamine, hyaluronic acid, chondroitin is now used as health food by many persons in Japan. The author will explain how hyaluronic acid, glucosamine, chondroitin is contributing to the health and anti-aging and long life. Japanese can live longest. Men 80.50 (third), women 86.63 (top). The reason of long life is Japanese eat many fish as protein source. Fish contain much hyaluronic acid, glucosamine and chondroitin, which precursor of anti-aging reagents. Fish production of Japan decreased remarkably to 10% since governments of developed country set up very strict law to eliminate NOx and NP in waste water. The author is proposing methods to control global warming by stopping NOx, NP in waste water elimination, we can increase the NP concentration of sea water. And we can increase plankton CO_2 fix, and we can protect global warming. And we can get many fish and we can enjoy long life.

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NOVEL PROPERTIES OF INDIVIDUAL MYOSIN HEADS IN SKELETAL MUSCLE AS REVEALED BY EXPERIMENTS USING THE GAS ENVIRONMENTAL CHAMBER

Haruo Sugi
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Although it is generally believed that muscle contraction results from ATP-driven cyclic attachment and detachment between myosin heads extending from myosin filaments and corresponding myosin-binding sites on actin filaments, the movement of myosin heads remains to be a matter for debate and speculation. The most straightforward way to visualize and record individual myosin head movement coupled with ATP hydrolysis is to use the carbon film-sealed gas environmental chamber (EC), which enables us to keep biological specimens like muscle actin and myosin filaments in wet, living state in the high vacuum of a transmission electron microscope. We have succeeded in recording ATP-induced movement of individual myosin heads, position-marked with gold particles (diameter, 20 nm) via site-directed antibodies to myosin head, and found novel properties of individual myosin heads, which are summarized as follows: In the absence of ATP, myosin heads take stable neutral position, around which they fluctuate. In the absence of actin filaments, individual myosin heads move away from, but not towards the bare region at the center of myosin filaments, i.e. they perform recovery stroke. After exhaustion of applied ATP return to their neutral position. The above finding indicates that myosin heads can sense the absence or presence of actin filament to determine their direction of ATP-induced movement, without being guided by actin filaments. In the presence of actin filaments, individual myosin heads perform power stroke in two different modes depending on experimental conditions. We emphasize that our EC experiment is the only method to visualize and record ATP-coupled movement of individual myosin heads, while all other methods can only obtain ambiguous results due to asynchronous nature of myosin head movement.

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THE DEVELOPMENT OF *ERBB2*-TARGETED THERAPY FOR ALZHEIMER'S DISEASE

Yung-Feng Liao, Bo-Jeng Wang, Yun-Wen Chen and Pei-Yi Wu
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g-Secretase-catalyzed production of amyloid-b (Ab) underlies the pathogenesis of Alzheimer's disease (AD). To identify genetic modifiers that can selectively affect g-secretase cleavage of APP while sparing notch cleavage, we generated cell-based assays employing bioluminescence resonance energy transfer (BRET) technology to monitor the protein-protein interactions between PS1 and two g-secretase substrates, APP C-terminal fragment (C99), and extracellular domain truncated notch (NΔE). An RNAi screen examining the effects of lentiviral shRNA clones targeting 777 kinases and 237 phosphatases encoded in the human genome identified 14 candidate genes whose downregulation resulted in a selective decrease in the interaction between PS1 and C99. Among those 14 candidate genes, an *ErbB2*-centered interaction network was found to be the most prominent regulatory signaling network that was predicted to preferentially govern the proteostasis of APP-C99. We further demonstrated that overexpression of *ErbB2* upregulates the levels of C99 and AICD effectively. The knockdown of *ErbB2* selectively decreased the protein levels of C99, AICD, and secreted Ab40, but not those of NΔE and NICD. Selective suppression of *ErbB2* expression by CL-387,785, an ErbB1/2-selective irreversible tyrosine kinase inhibitor, can preferentially attenuate the levels of C99 and AICD, resulting in a significant reduction in Ab production. Down-regulation of *ErbB2* by CL-387,785 also resulted in a significant decrease in the levels of C99 and secreted Aβ in both zebrafish and mouse models of AD, through the activation of autophagy. Oral administration of CL-387,785 for 3 wk significantly improves the cognitive functions of APP/presenilin-1 (PS1) transgenic mice. These findings unveil a noncanonical function of *ErbB2* in modulating autophagy and establishe *ErbB2* as a novel therapeutic target for AD.