GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 6 (351) Июнь 2024

ТБИЛИСИ - NEW YORK

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии
საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press. Published since 1994. Distributed in NIS, EU and USA.

GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.
GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.
ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

**Articles that Fail to Meet the Aforementioned
Requirements are not Assigned to be Reviewed.**

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman** (**Кириллица**), ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

GEORGIAN MEDICAL NEWS
No 6 (351) 2024

Содержание:

Tan Minh Hoang, Hung Dinh Kieu, Vu Nguyen, Trung Kien Tran, Tan Chor Ngee, Ha Dai Duong.
CLINICAL AND IMAGING OUTCOMES OF XLIF SURGERY FOR LUMBAR SPINAL STENOSIS…….............................……….6-11

Nino Totadze, Rishu Bansal.
NUTRITION AND PHYSICAL ACTIVITY OF PREGNANT WOMEN INCLUDING BARIATRIC SURGERY……………...………….12-17

Arpine Muradyan.
THE EFFECT OF DIFFERENT FITNESS TRAINING PROGRAMS AND FREQUENCY ON HEALTH-RELATED QUALITY OF LIFE……
……………………………..………………………………………………………………...……….18-22

Serhii Terekhov, Andrii Proshchenko, Nina Proshchenko.
ANALYSIS OF THE USE OF COMPLEX DIGITAL TECHNOLOGIES IN THE DIAGNOSIS AND TREATMENT OF OCCLUSAL ANOMALIES………………………………………………………………………………….........................……………………….23-32

Vahe Ashot Ter-Minasyan.
FERTILITY FUNCTIONS IN 4VHPV VACCINATED ARMENIAN COHORT………………..........................………………..……33-37

Alaa S. Mahdi, Ahmed H. Salman, Zahraa K. Al-Hassani, Hayder A.H. Jalil.
DECODING PEDIATRIC MENINGITIS UNRAVELING THE INTRICACIES OF ANTIMICROBIAL RESISTANCE IN IRAQI PEDIATRIC PATIENTS……………………………………………………………………...……………………….38-43

Rajab A. Alzahrani, Soliman shreed Soliman, Saadi Rabea Saadi AlGhamdi, Mohammed Abdullah S Alzahrani, Abdullah Mohammed B Alghamdi, Ibrahim Abdulaziz A Alghamdi, Essam Mohammed S Alghamdi, Musab Mohammed B Alzahrani, Yahya Ahmed Salem Alzahrani, Mujtaba Alrayah Fadlalla, Mohammed A. Alghamdi.
EFFECT OF ENLARGED ADENOIDS AND TONSILS ON BLOOD OXYGEN SATURATION IN AL BAHA, SAUDI ARABIA……………………………...……………………..44-48

Sivakumar Palanisamy, Priyatharshni Subramani, Prabhu Narasimman, Manikkampatti Palanisamy Murugesan.
ADVANCEMENT IN ALPHA-SYNUCLEIN PROTEOMICS: EXPLORING ANALYTICAL TECHNIQUES AND THEIR CLINICAL IMPLICATIONS IN PARKINSON'S DISEASE………………………..…………………………….49-54

Teremetskyi VI, Frolova OH, Batryn OV, Myrza SS, Matviichuk AV, Ryzhenko OS.
VECTORS OF DEVELOPMENT OF THE UNIFIED MEDICAL INFORMATION SPACE……...............................…………………….55-60

Rajaa Hussein Fayadh, Rawnaq Thamer Kadium, H. N. K. AL-Salman, Falah Hassan Shari.
HPLC METHOD FOR THE QUANTIFICATION OF SOME ACTIVE FLAVONOIDS IN ETHYL ACETATE EXTRACT OF LEAVES OF BUTEA *MONOSPERMA* LINN……………………………………………..……………….61-64

Tchernev G, Ivanov L, Broshtilova V.
MULTIPLE KERATINOCYTIC CANCERS AFTER INTAKE OF ANTIHYPERTENSIVES (LISINOPRIL/ BISOPROLOL/HCT) AND ANTIARRHYTMICS (PROPAFENONE): THE IMPORTANT NEW LINKS TO THE NITROSO-CONTAMINATION AND THE METABOLIC REPROGRAMMING OF THE FUTURE CANCER CELL………………………………………………………………...65-71

Maryam A. Faiq, Nehad N. Hilal, Mohammed T. Dawood.
LEVELS OF OSTEOPROTEGERIN AND IRISIN IN POSTMENOPAUSAL OSTEOPOROSIS WOMEN…..…………………………….72-75

Tianhua Du, Guangren Zhou, Shouzhi Wu, Haining Ni.
UNDERSTAND THE CURRENT SITUATION OF STUDENTS' PHYSICAL FITNESS TEST AND MEASURES TO IMPROVE THEIR PHYSICAL FITNESS TEST SCORES………………………………………………...…………………….76-79

Sosonna L.O, Boiagina O.D, Yurevych N.O, Schevtsov O.O, Avilova O.V, Konoval N.S, Sukhina I.S.
INDIVIDUAL ANATOMICAL VARIABILITY OF THE ANTEROPOSTERIOR LATERAL DIMENSIONS OF THE FACIAL SKULL IN MATURE ADULTS…………………………………………………………………...…………………..…80-84

Zhanat Ispayeva, Raikhan Bekmagambetova, Mereke Mustafina, Elena Kovzel, Galiya Tusupbekova, Marina Morenko, Timur Saliev, Shynar Tanabayeva, Ildar Fakhradiyev.
RELIABILITY AND VALIDITY OF THE KAZAKH-LANGUAGE ACT QUESTIONNAIRE AS AN ASTHMA CONTROL TOOL.......85-90

Khitaryan D.S, Stepanyan L.S, Khachatryan M.M, Barbaryan M.S.
JUDO AS AN ALTERNATIVE INTERVENTION MODEL TO PREVENT BULLYING AT SCHOOLS: A PILOT STUDY……………..91-95

Rania M. Tuama, Entedhar R. Sarhat.
THE ROLE OF MYONECTIN IN PATIENTS WITH TYPE 2 DIABETES MELLITUS…………………………….................................96-99

Rongmin Xu,Shundong Li, Anhua Zheng, Lianping He.
EFFECT OF XIAOYAO PILLS COMBINED WITH ALENDRONATE ON BONE DENSITY IN POSTMENOPAUSAL PATIENTS WITH OSTEOPOROSIS……………………………………………...……………100-101

Nino Kiria, Teona Avaliani, Nino Bablishvili, Nino Chichiveishvili, Giorgi Phichkhaia, Lali Sharvadze, Nana Kiria.
EFFICACY AND SAFETY OF SILVER NANOCOMPOSITES ON RIFAMPICIN-RESISTANT M. TUBERCULOSIS STRAI NS……………………………................……………………………………………………………………………………………102-108

Dubivska S.S, Hryhorov Y.B, Lazyrskyi V.O, Dotsenko D.G, Lebid P.B.
THE INFLUENCE OF CHANGES IN CARBOHYDRATE METABOLISM INDICATORS IN PATIENTS WITH POLYTRAUMA COMPLICATED BY ALCOHOLIC DELIRIUM ON THE CHOICE OF THE SEDATION METHOD……………….....……………….109-115

Karapetyan A.G, Danielyan M.H, Badalyan B.Yu, Simonyan K.V, Grigoryan V.S, Simonyan M.A, Dallakyan A.M, Simonyan G.M, Simonyan R.M.
PROTECTIVE EFFECT OF A NEW SUPEROXIDE-PRODUCING ENZYME COMPLEX FROM RASPBERRY IN RATS WITH THIRD-DEGREE THERMAL BURNS...……………………………………………………………………..116-124

Sura Z. Salih, Nehad N. Hilal.
EVALUATION OF SERUM VASPIN LEVEL IN IRAQI WOMEN WITH GESTATIONAL DIABETES MELLITUS…....……………125-130

Tchernev G, Ivanov L.
MUSTARDE ROTATION FLAP AS ADEQUATE OPTION FOR HIGH-RISK BCC NEAR THE LOWER EYE LID: THE ADDITIONAL INTAKE OF N-NITROSO-FOLIC-ACID AND N-NITROSO-RIVOROXABAN AS COFACTORS/ TRIGGERS OF THE METABOLIC REPROGRAMMING OF THE FUTURE CANCER CELL…................................……………………………………………………131-137

Nazym Ailbayeva, Aliya Alimbaeva, Saule Rakhyzhanova, Nazym Kudaibergenova, Duman Berikuly, Sayat Tanatarov, Zaure Dushimova, Timur Saliev, Shynar Tanabayeva, Sergey Lee, Ildar Fakhradiyev.
THE IMPACT OF BIRTH WEIGHT ON INFANT MORTALITY IN KAZAKHSTAN…………….................................………………..138-145

Voloshyn-Gaponov I.K, Lantukh I.V, Mikhanovska N.G, Gulbs O.A, Malieieva O.V, Dikhtiarenko S.Yu, Kobets O.V, Malieiev D.V.
PSYCHOTHERAPEUTICAL FEATURES OF PERSONS WITH MULTIPLE SCLEROSIS AND HEPATOCEREBRAL DEGENERATION...146-151

Sevak Sanasar Shahbazyan.
COMPARATIVE ANALYSIS OF EFFECTS INDUCED BY STANDARD AND MODIFIED LAPAROSCOPIC SLEEVE GASTRECTOMY PERFORMANCE ON SHORT TERM AND DISTAL COMPLICATIONS IN PATIENTS WITH 3RD DEGREE OF MORBID OBESITY………………………………………...……………………………………152-157

Qutaiba A. Qasim.
ANTIOXIDANTS, LIPID PROFILES, AND GLUCOSE LEVELS, AS WELL AS PERSISTENT INFLAMMATION, ARE CENTRAL TO THE LINK BETWEEN DIABETES MELLITUS TYPE II AND OXIDATIVE STRESS………..…………..157-161

Stepanyan L.S, Khitaryan D.S.
RESEARCH ON PSYCHOLOGICAL WELL-BEING AND EMOTIONAL PROFILE OF ADOLESCENTS IN THE CONTEXT OF SCHOOL BULLYING………………………………………...………………………………………………..162-166

Yi Jin, Zhi Luo, Hua-Qin Su, Cui-Ping Li, Cai-Li Wang, Li-Fen Zhang, Feng-Lian Peng, Lian-Ping He, Xiang-Hu Wang.
SERUM CALCIUM WAS NEGATIVELY ASSOCIATED WITH SERUM IRON AMONG GENERAL POPULATION: FINDINGS FROM A CROSS-SECTIONSTUDY…………………………………………...……………167-169

Stela Dzotsenidze, Lali Pkhaladze, Jenaro Kristesashvili, Nina Davidovi, Samer Hammoude, Marika Zurmukhtashvili.
FUNCTIONAL STATE OF THE REPRODUCTIVE SYSTEM AFTER UNILATERAL OOPHORECTOMY…………......……………170-174

GEORGIAN MEDICAL NEWS
No 6 (351) 2024

ADVANCEMENT IN ALPHA-SYNUCLEIN PROTEOMICS: EXPLORING ANALYTICAL TECHNIQUES AND THEIR CLINICAL IMPLICATIONS IN PARKINSON'S DISEASE

Sivakumar Palanisamy[1,2]*, Priyatharshni Subramani[3], Prabhu Narasimman[3], Manikkampatti Palanisamy Murugesan[4].

[1]R&D Laboratory, Department of Chemistry, Excel Engineering College (Autonomous), Namakkal – 637 303, Tamil Nadu, India.

[2]CAS Key Laboratory of Separation Science for Analytical Chemistry, Dalian Institute of Chemical Physics, No-457 Zhongshan Road, Dalian – 116 023, P.R. China.

[3]R&D Laboratory, Department of Physics, Excel Engineering College (Autonomous), Namakkal – 637 303, Tamil Nadu, India.

[4]Department of Food Technology, Excel Engineering College (Autonomous), Namakkal – 637 303, Tamil Nadu, India.

Abstract.

Parkinson's disease (PD) is a prevalent neurodegenerative disorder, affecting around 500,000 to 1 million Americans, with a significant portion diagnosed before age 50. Despite advances in treatments such as dopamine replacement therapy and deep brain stimulation, no therapies currently exist to halt or slow disease progression in advanced stages. Research is increasingly focused on identifying early biomarkers for PD to enable earlier intervention. Alpha-synuclein (α-Syn), a key protein implicated in PD pathology, is studied using various proteomics techniques like mass spectrometry, gel electrophoresis, and chromatography, to understand its role and alterations in PD. These techniques help in extracting, analyzing, and characterizing α-Syn from brain samples, providing insights into disease mechanisms and potential diagnostic and therapeutic applications.

Key words. Parkinson's disease, alpha-synuclein, analytical techniques, biomarkers, clinical implications.

Introduction.

Parkinson's Disease.

Parkinson's disease (PD) is the second-most common neurodegenerative disorder in the United States, following Alzheimer's disease [1]. Although most people are diagnosed with PD at age 60 or older, approximately 5 to 10 percent receive a diagnosis before age 50 [2]. Current estimates suggest that around 500,000 Americans are diagnosed with PD, though some experts believe the actual number may be as high as 1 million [3]. Projections indicate that these figures could double by the year 2040.

Over the decades, numerous treatment options have been developed worldwide to address the motor symptoms associated with PD. Dopamine (DA) replacement therapy, utilizing medications such as Sinemet and levodopa, remains a cornerstone of PD treatment and has proven effective, particularly in the early stages of the disease [4]. Additionally, deep brain stimulation has shown promise in reducing tremors, rigidity, and improving movement in PD patients [5]. However, despite these advancements, significant challenges persist, as there are currently no therapies available to slow down disease progression or alleviate symptoms in advanced PD stages.

Further research is crucial for enhancing our understanding of PD pathology, particularly in its preclinical phase. Priority should be placed on identifying biological markers, or biomarkers, that can detect PD in its early stages, thus enabling early intervention and risk mitigation. The development of highly sensitive and specific analytical methods capable of detecting PD biomarkers in preclinical samples will be essential for future advancements in this area. This review will focus on the analytical techniques for extracting and analyzing PD biomarkers in brain tissue samples.

Biomarkers and their Role in PD Pathology.

Parkinson's disease (PD) manifests when neurons within the central nervous system or elsewhere in the nervous system malfunction or undergo cell death [2]. Key symptoms include bradykinesia, tremors, postural instability, and rigidity, primarily stemming from neuron loss in the substantia nigra, a critical region in the midbrain responsible for motor control.

Dopamine (DA), a neurotransmitter produced in the substantia nigra, plays a crucial role in synaptic signal transmission essential for bodily movement [1]. An abnormal concentration of DA disrupts signal transmission, impairing movement. At PD diagnosis, individuals typically exhibit a loss of approximately 60 to 80 percent of DA-producing cells in the substantia nigra [2]. Recent studies indicate that besides DA, neurotransmitters like norepinephrine, serotonin, and acetylcholine, which regulate nervous signal transmission, also experience alterations in concentration, affecting brain structure and chemical pathways, potentially contributing to PD's non-motor features.

Furthermore, abnormalities in alpha-synuclein (α-Syn) are believed to be pivotal in PD development. α-Syn is a component of presynaptic neuron terminals where neurotransmitters are released for interneuronal signaling [6]. Excessive buildup of α-Syn in presynaptic neurons is implicated in PD pathogenesis. Certain genetic mutations in α-Syn within families lead to misfolding of its structure, resulting in accumulation and aggregation of misfolded α-Syn into fibrils. These fibrils serve as the building blocks of Lewy bodies, abnormal structures forming inside nerve cells of the substantia nigra, ultimately affecting normal function and triggering nerve cell death, characteristic of PD [7].

Proteomics of Alpha-Synuclein Biomarkers.

The study of alpha-synuclein (α-Syn) proteomics in Parkinson's disease (PD) has garnered significant attention in recent years [8]. Proteomics techniques enable the comprehensive analysis of proteins, including α-Syn, in biological samples, offering insights into their abundance, post-translational modifications, and interactions within cellular pathways [9].

Several studies have employed mass spectrometry-based proteomics to investigate α-Syn levels and modifications in PD. These approaches have identified specific α-Syn isoforms and post-translational modifications, such as phosphorylation, nitration, and truncation, which may influence α-Syn aggregation

and toxicity [10]. Furthermore, quantitative proteomics studies have revealed alterations in α-Syn-associated protein networks in PD brains, shedding light on potential biomarkers and therapeutic targets [11].

In addition to mass spectrometry, other proteomics techniques, including immunoassays and protein microarrays, have been utilized to assess α-Syn levels in biological fluids such as cerebrospinal fluid and blood plasma [12]. These studies aim to identify reliable biomarkers for PD diagnosis, prognosis, and monitoring disease progression.

Overall, proteomics approaches offer valuable tools for investigating α-Syn biology and its implications in PD pathogenesis. Continued advancements in proteomic technologies hold promise for uncovering novel insights into α-Syn-related mechanisms and facilitating the development of precision diagnostics and therapeutics for PD [13].

Analytical Techniques Involved in the Proteomics of Alpha-Synuclein Biomarkers.

The proteomic investigation of alpha-synuclein (α-Syn) biomarkers in Parkinson's disease (PD) involves a range of analytical techniques for sample preparation, separation, extraction, and identification [14] as shown in Figure 1.

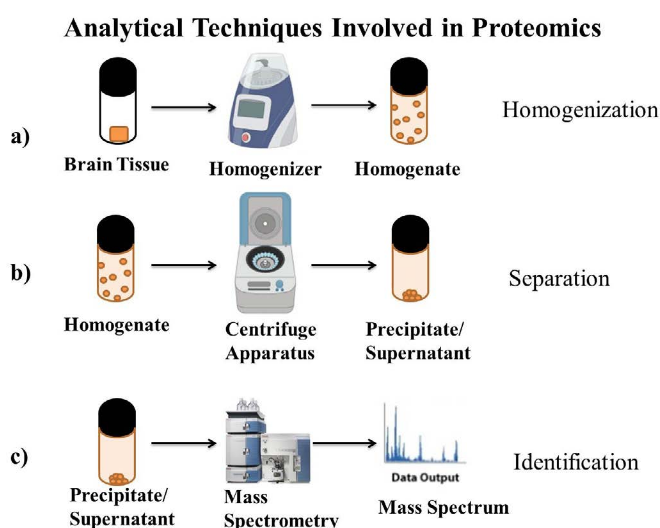

Figure 1. *Schematic diagram for the homogenization, separation and identification of α-Syn from brain tissue samples.*

Homogenization.

Traditional Homogenization Methods: Sonication involves the application of high-frequency sound waves to disrupt cellular structures and release α-Syn from tissues or cells [15]. While effective in some cases, sonication may result in protein denaturation or aggregation, affecting the accuracy of α-Syn quantification. Mechanical methods, such as bead beating or grinding, rely on physical force to break down tissues and cells [16]. These techniques are widely used due to their simplicity and effectiveness but may require optimization to ensure consistent α-Syn extraction and minimal degradation.

Enzymatic Homogenization: Proteinase K treatment selectively digests cellular proteins while preserving α-Syn integrity [17]. This enzymatic approach efficiently releases α-Syn from complex biological matrices, making it suitable for biomarker analysis in cerebrospinal fluid (CSF) and brain tissues. Trypsin digestion can be employed to fragment proteins and improve the solubility of α-Syn aggregates [18]. Combined with subsequent mass spectrometry analysis, trypsinization enables detailed characterization of α-Syn isoforms and post-translational modifications.

Detergent-Based Homogenization: Detergent-based methods involve the use of non-ionic detergents to solubilize α-Syn aggregates and membrane-bound proteins [19]. Triton X-100 or NP-40 extraction is commonly used for α-Syn isolation from cell cultures or tissue lysates, facilitating downstream biochemical analyses. Sarkosyl, a mild detergent, can selectively solubilize α-Syn aggregates while preserving their native conformation [20]. Sarkosyl extraction is particularly valuable for isolating insoluble α-Syn species from post-mortem brain samples, providing insights into pathological mechanisms underlying PD.

Novel Homogenization Approaches: Microfluidization utilizes high-pressure homogenization to achieve uniform particle size reduction and efficient protein extraction [21]. This emerging technique shows promise for preserving α-Syn structure and improving the reproducibility of biomarker quantification in biological fluids and tissues. Ultracentrifugation-based methods, such as density gradient centrifugation, enable the isolation of α-Syn aggregates based on their buoyant density [22]. By separating soluble and insoluble α-Syn fractions, ultracentrifugation facilitates the characterization of pathological α-Syn conformers associated with PD progression. The different types of homogenization methods and their outcome are listed in Table 1.

Separation.

Gel Electrophoresis: Sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) separates proteins based on their molecular weight under denaturing conditions [23]. This technique is widely used to detect and quantify α-Syn monomers and oligomers in cell lysates, tissue extracts, and biological fluids.

Chromatographic Techniques: Size-Exclusion Chromatography (SEC) separates proteins based on their size and molecular weight by allowing smaller molecules to enter the porous stationary phase, while larger molecules elute first [24]. SEC is valuable for analyzing α-Syn oligomerization and aggregation states in biological samples. Ion-Exchange Chromatography (IEC) separates proteins based on their net charge, exploiting differences in their ionic interactions with the stationary phase [25]. This technique can be utilized for the purification and fractionation of α-Syn isoforms and post-translationally modified forms. Reversed-Phase Chromatography (RPC) separates proteins according to their hydrophobicity, with more hydrophobic proteins eluting later [26]. RPC coupled with mass spectrometry allows for the identification and characterization of α-Syn variants and modifications.

Immunoprecipitation (IP) and Affinity Capture: IP utilizes specific antibodies to selectively capture α-Syn from complex biological samples, followed by elution and downstream analysis

Table 1. Different homogenization techniques and their outcomes [15-22].

S. No.	Type	Method	Outcome	Reference (s)
1.	Traditional Homogenization Methods	Sonication	It results in protein denaturation or aggregation, affecting the accuracy of α-Syn quantification.	[15]
		Mechanical Homogenization	It requires optimization to ensure consistent α-Syn extraction and minimal degradation.	[16]
2.	Enzymatic Homogenization	Proteinase K Digestion	It efficiently releases α-Syn from complex biological matrices, making it suitable for biomarker analysis in cerebrospinal fluid (CSF) and brain tissues.	[17]
		Tripsinization	It enables detailed characterization of α-Syn isoforms and post-translational modifications in combined with mass spectrometry.	[18]
3.	Detergent Based Homogenization	Triton-X or NP-40 Extraction	It is commonly used for α-Syn isolation from cell cultures or tissue lysates, facilitating downstream biochemical analyses.	[19]
		Sarkosyl Extraction	It is particularly valuable for isolating insoluble α-Syn species from post-mortem brain samples, providing insights into pathological mechanisms underlying PD.	[20]
4.	Novel Homogenization	Microfluidization	It shows promise for preserving α-Syn structure and improving the reproducibility of biomarker quantification in biological fluids and tissues.	[21]
		Ultracentrifugation	It facilitates the characterization of pathological α-Syn conformers associated with PD progression by separating soluble and insoluble α-Syn fractions.	[22]

[27]. This technique enables the enrichment and detection of α-Syn in low-abundance samples, such as cerebrospinal fluid (CSF) or blood plasma. Affinity chromatography utilizes immobilized ligands, such as antibodies or aptamers, to selectively bind and isolate α-Syn from sample matrices [28]. This approach offers high specificity and purity, facilitating the analysis of α-Syn interactions and modifications.

Mass Spectrometry (MS)-Based Techniques: Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) analyzes α-Syn peptides or protein fragments based on their mass-to-charge ratio [29]. MALDI-TOF MS is employed for profiling α-Syn isoforms and PTMs in biological samples. Liquid chromatography-tandem mass spectrometry (LC-MS/MS) combines chromatographic separation with mass spectrometric detection, allowing for the identification and quantification of α-Syn peptides with high sensitivity and accuracy [30]. LC-MS/MS is instrumental in elucidating α-Syn proteoforms and their dynamics in PD pathology. The different types of separation techniques and their outcome are listed in Table 2.

Identification/Imaging.

Mass Spectrometry-Based Techniques: Peptide Mass Fingerprinting (PMF) involves enzymatic digestion of α-Syn followed by mass spectrometry analysis to generate a peptide mass fingerprint [14]. Comparison of experimental peptide masses with theoretical masses allows for the identification of α-Syn and its post-translational modifications (PTMs). Tandem Mass Spectrometry (MS/MS) fragmentation of α-Syn peptides enables the determination of its amino acid sequence and characterization of PTMs [15]. This technique provides valuable insights into α-Syn structure and function, aiding in the understanding of PD pathology. Shotgun proteomics combines enzymatic digestion of α-Syn with liquid chromatography-tandem mass spectrometry (LC-MS/MS) to identify and quantify α-Syn and its interacting partners in complex biological samples [28]. Shotgun proteomics facilitates comprehensive characterization of α-Syn proteoforms and their roles in PD pathogenesis.

Antibody-Based Techniques: Immunohistochemistry (IHC) utilizes α-Syn-specific antibodies to detect and localize α-Syn aggregates in tissue sections [24]. This technique is valuable for visualizing α-Syn pathology in post-mortem brain samples and identifying cellular and subcellular localization patterns associated with PD. Immunoblotting, or Western blotting, employs α-Syn antibodies to detect and quantify α-Syn monomers and oligomers in cell lysates or tissue homogenates [29]. Immunoblotting is widely used for semi-quantitative analysis of α-Syn expression levels and aggregation states.

Imaging Techniques: Immunofluorescence (IF) combines α-Syn-specific antibodies with fluorescent dyes to visualize α-Syn localization and distribution in cultured cells or tissue sections [24]. IF allows for the assessment of α-Syn aggregation and subcellular localization dynamics in PD models. Positron emission tomography (PET) imaging utilizes radiolabeled ligands to visualize α-Syn aggregates in living brains of PD patients [30]. PET imaging provides non-invasive insights into α-Syn pathology and disease progression, facilitating early diagnosis and monitoring of PD.

Emerging Techniques: Single-molecule imaging techniques, such as single-molecule fluorescence microscopy, enable the visualization and tracking of individual α-Syn molecules in real-time [29]. Single-molecule imaging offers unprecedented spatial and temporal resolution for studying α-Syn aggregation kinetics and protein dynamics. Proximity Ligation Assay (PLA) detects protein-protein interactions, including α-Syn interactions with other cellular components, by amplifying the signal generated from close proximity of two target proteins [30]. PLA is

Table 2. Different separation techniques and their outcomes [23-30].

S. No.	Type	Method	Outcome	Reference (s)
1.	Gel Electrophoresis	SDS-PAGE	It is widely used to detect and quantify α-Syn monomers and oligomers in cell lysates, tissue extracts, and biological fluids.	[23]
2.	Chromatographic Techniques	Size-Exclusion Chromatography (SEC)	It is valuable for analyzing α-Syn oligomerization and aggregation states in biological samples.	[24]
		Ion Exchange Chromatography	It can be utilized for the purification and fractionation of α-Syn isoforms and post-translationally modified forms.	[25]
		Reversed Phase Chromatography	It coupled with mass spectrometry allows for the identification and characterization of α-Syn variants and modifications.	[26]
3.	Immunoprecipitation (IP) and Affinity Capture	Antibody based IP	It enables the enrichment and detection of α-Syn in low-abundance samples, such as cerebrospinal fluid (CSF) or blood plasma.	[27]
		Affinity Chromatography	It offers high specificity and purity, facilitating the analysis of α-Syn interactions and modifications.	[28]
4.	Mass Spectrometry (MS) Based Techniques	MALDT-TOF-MS	It is employed for profiling α-Syn isoforms and PTMs in biological samples.	[29]
		LC-MS/MS	It combines chromatographic separation with mass spectrometric detection, allowing for the identification and quantification of α-Syn peptides with high sensitivity and accuracy.	[30]

Table 3. Different identification/imaging techniques and their outcomes [14,15, 24,25,27-30].

S. No.	Type	Method	Outcome	Reference (s)
1.	Mass Spectrometry Based Techniques	Peptide Mass Fingerprinting (PMF)	By comparing experimental peptide masses with theoretical masses, it allows for the identification of α-Syn and its post-translational modifications (PTMs).	[14]
		Tandem Mass Spectrometry (MS/MS)	It provides valuable insights into α-Syn structure and function, aiding in the understanding of PD pathology.	[15]
		Shotgun Proteomics	It combines enzymatic digestion of α-Syn with liquid chromatography-tandem mass spectrometry (LC-MS/MS) to identify and quantify α-Syn and its interacting partners in complex biological samples	[25]
2.	Antibody Based Techniques	Immunohistochemistry	It is valuable for visualizing α-Syn pathology in post-mortem brain samples and identifying cellular and subcellular localization patterns associated with PD.	[27]
		Immunoblotting	It employs α-Syn antibodies to detect and quantify α-Syn monomers and oligomers in cell lysates or tissue homogenates.	[30]
3.	Imaging Techniques	Immunofluorescence	It combines α-Syn-specific antibodies with fluorescent dyes to visualize α-Syn localization and distribution in cultured cells or tissue sections.	[28]
		PET imaging	It provides non-invasive insights into α-Syn pathology and disease progression, facilitating early diagnosis and monitoring of PD.	[24]
4.	Emerging Techniques	Single Molecule Imaging	It offers unprecedented spatial and temporal resolution for studying α-Syn aggregation kinetics and protein dynamics.	[29]
		Proximity Ligation Assay (PLA)	It detects protein-protein interactions, including α-Syn interactions with other cellular components, by amplifying the signal generated from close proximity of two target proteins.	[30]

valuable for studying α-Syn interactions and their implications in PD pathogenesis. The different types of separation techniques and their outcome are listed in Table 3.

Clinical Applications of Alpha-Synuclein Biomarkers.

α-Syn has garnered significant interest as a biomarker in the clinical management of PD and other neurodegenerative disorders. The protein's role in disease pathology and its presence in various body fluids and tissues have led to its exploration across several clinical applications. This section will delve into the potential uses of α-Syn biomarkers in early diagnosis, differential diagnosis, monitoring disease progression, and assessing therapeutic response.

Early Diagnosis: The early diagnosis of PD is crucial, as neurodegeneration often precedes clinical symptoms by several years. Traditional diagnostic methods rely on clinical signs and symptoms, which typically appear after significant neuronal loss has already occurred. α-Syn biomarkers offer the potential to detect the disease at a much earlier stage [32].

Prodromal Biomarkers: The presence of α-Syn aggregates in peripheral tissues, such as skin, olfactory neurons, or the gastrointestinal tract, has been observed in individuals who are still asymptomatic but are at high risk for PD. These findings suggest that α-Syn could be a biomarker for prodromal PD, allowing for the identification of individuals before the onset of motor symptoms. Early intervention strategies could then be applied to slow or alter the course of the disease.

Screening for At-Risk Populations: In individuals with known risk factors (e.g., genetic predisposition, rapid eye moment (REM) sleep behaviour disorder, or hyposmia), screening for α-Syn in accessible tissues or fluids could help identify those at the highest risk of developing PD. This approach could be particularly valuable in clinical trials aimed at testing disease-modifying therapies in pre-symptomatic individuals.

Differential Diagnosis: PD shares many clinical features with other neurodegenerative disorders, such as Multiple System Atrophy (MSA), Dementia with Lewy Bodies (DLB), and Alzheimer's Disease (AD). However, these conditions have different pathophysiological mechanisms, prognoses, and treatment approaches. Accurate differential diagnosis is, therefore, essential for optimal patient management [31].

Distinguishing PD from MSA and DLB: Although MSA and DLB are also synucleinopathies, the distribution and form of α-Syn pathology differ from that in PD. For example, in MSA, α-Syn aggregates are primarily found in oligodendrocytes rather than neurons. Biomarkers that distinguish between neuronal and oligodendroglial α-Syn could be instrumental in differentiating these diseases.

AD *vs.* PD with Dementia (PDD): In clinical settings where distinguishing between AD and PDD is challenging, α-Syn biomarkers, when combined with other biomarkers (e.g., tau and amyloid-beta), can improve diagnostic accuracy. Elevated levels of α-Syn in CSF or reduced levels in plasma have been observed in PD and PDD, offering a contrast to the typical biomarker profile seen in AD.

α-Syn and Tau/Amyloid-Beta Ratios: Recent studies have explored the use of ratios between α-Syn and other neurodegenerative biomarkers, such as tau and amyloid-beta, to enhance diagnostic precision. This approach may help clinicians differentiate between pure synucleinopathies and mixed pathologies that involve both tau and amyloid pathology.

Monitoring Disease Progression.

As PD progresses, patients typically experience a gradual worsening of motor and non-motor symptoms. Monitoring disease progression is vital for evaluating the effectiveness of therapeutic interventions and adjusting treatment plans accordingly. α-Syn biomarkers have the potential to serve as indicators of disease progression [33].

Longitudinal Biomarker Changes: Studies have shown that levels of oligomeric or phosphorylated α-Syn in CSF and blood may change as the disease progresses. For instance, an increase in CSF oligomeric α-Syn has been correlated with the severity of motor symptoms and cognitive decline in PD patients. By regularly monitoring these biomarkers, clinicians can gain insights into disease progression at a molecular level, beyond what is visible through clinical assessment alone.

Stage-Specific Biomarkers: The development of stage-specific α-Syn biomarkers could allow for a more nuanced understanding of disease progression. For example, certain forms of α-Syn might be more prevalent in early versus late stages of PD, providing a timeline of molecular changes that correspond to clinical stages.

Prognostic Value: α-Syn biomarkers could also offer prognostic information, helping to predict the rate of disease progression in individual patients. This could be particularly valuable in stratifying patients for clinical trials or tailoring treatment strategies to slow disease progression.

Response to Therapy.

As the focus of PD treatment shifts from symptomatic management to disease modification, there is a growing need for biomarkers that can accurately reflect treatment response. α-Syn biomarkers hold promise in this regard, particularly in evaluating the efficacy of therapies aimed at reducing α-Syn aggregation or enhancing its clearance [34].

Measuring Treatment Efficacy: In clinical trials, α-Syn biomarkers could serve as surrogate endpoints, allowing for the early assessment of treatment efficacy. For example, a decrease in CSF or plasma oligomeric α-Syn levels following treatment could indicate a reduction in pathological α-Syn burden, even before clinical improvements are evident.

Targeted Therapies: Therapies targeting α-Syn, such as immunotherapies (e.g., monoclonal antibodies against α-Syn), gene therapies, or small molecules that inhibit aggregation, could benefit from α-Syn biomarkers to track their effects in real-time. These biomarkers could help determine the optimal dosing and timing of such treatments.

Personalized Medicine: By integrating α-Syn biomarkers into clinical practice, clinicians could adopt a more personalized approach to PD treatment. For instance, patients with higher levels of oligomeric α-Syn might respond better to therapies that specifically target these toxic species, leading to more tailored and effective interventions.

Conclusion.

The proteomic investigation of α-Syn biomarkers in PD has become increasingly prominent, employing advanced

proteomics techniques to explore the abundance, modifications, and interactions of α-Syn within biological samples. Mass spectrometry-based proteomics has been particularly valuable in identifying specific α-Syn isoforms and post-translational modifications, such as phosphorylation and nitration, which are believed to influence α-Syn's aggregation and toxicity. Moreover, quantitative proteomics studies have revealed significant alterations in α-Syn-associated protein networks in PD brains, offering insights into potential biomarkers and therapeutic targets. Besides mass spectrometry, other techniques like immunoassays and protein microarrays are used to assess α-Syn levels in cerebrospinal fluid and blood plasma, aiming to develop reliable biomarkers for PD diagnosis and monitoring. These proteomics approaches are pivotal in understanding α-Syn biology and its role in PD pathogenesis, holding promise for the development of precision diagnostics and therapeutics tailored to PD.

Conflict of Interest.

All authors have reviewed and approved this publication. They collectively declare no conflicts of interest associated with this research endeavor.

REFERENCES

1. National Institute of Neurological Disorders and Stroke. (n.d.). Parkinson's Disease Information Page. https://www.ninds.nih.gov/Disorders/All-Disorders/Parkinsons-Disease-Information-Page.
2. Kalia L.V, Lang A.E. Parkinson's disease. The Lancet. 2015;386:896-912.
3. Dorsey E.R, Constantinescu R, Thompson J.P, et al. Projected number of people with Parkinson disease in the most populous nations, 2005 through 2030. Neurology. 2007;68:384-386.
4. Connolly B.S, Lang A.E. Pharmacological treatment of Parkinson disease. JAMA. 2014;311:1670-1683.
5. Weaver F.M, Follett K, Stern M, et al. Bilateral deep brain stimulation vs best medical therapy for patients with advanced Parkinson disease: a randomized controlled trial. JAMA. 2009;301:63-73.
6. Spillantini M.G, Schmidt M.L, Lee V.M, et al. α-Synuclein in Lewy bodies. Nature. 1997;388:839-840.
7. Polymeropoulos M.H, Lavedan C, Leroy E, et al. Mutation in the α-synuclein gene identified in families with Parkinson's disease. Science. 1997;276:2045-2047.
8. Cookson M.R. α-Synuclein and neuronal cell death. Molecular Neurodegeneration. 2009;4:9.
9. Yates J.R, Ruse C.I, Nakorchevsky A. Proteomics by mass spectrometry: approaches, advances, and applications. Annu Rev Biomed Eng. 2009;11:49-79.
10. Fujiwara H, Hasegawa M, Dohmae N, et al. α-Synuclein is phosphorylated in synucleinopathy lesions. Nature Cell Biology. 2002;4:160-164.
11. Xicoy H, Wieringa B, Martens G.J, et al. Quantitative proteomics of synaptosomal fractions in a rat overexpressing human α-synuclein. Scientific Reports. 2017;7:1-12.
12. Mollenhauer B, Locascio J.J. Amino terminally truncated α-synuclein as a potential biomarker for Parkinson's disease. Science Translational Medicine. 2011;4:121ra20.
13. Emamzadeh F.N. α-Synuclein structure, functions, and interactions. Journal of Research in Medical Sciences. 2016;21:29.
14. Smejkal GB, Robinson MB. Nervous system tissue preparation for immunohistochemistry. J Vis Exp. 2010;41:2021.
15. de Planell-Saguer M, Rodicio MC. Analytical aspects of microRNA in diagnostics: A review. Anal Chim Acta. 2011;699:134-152.
16. Schosserer M, Grillari J, Breitenbach M. The dual role of cellular senescence in developing tumors and their response to cancer therapy. Front Oncol. 2017;7:278.
17. McPherson PS, Garcia EP, Slepnev VI, et al. A presynaptic inositol-5-phosphatase. Nature. 1996;379:353-357.
18. Wheeler DS, Barrick SR, Grubisha MJ, et al. Direct interaction between NHERF1 and Frizzled regulates β-catenin signaling. Oncogene. 2011;30:32-42.
19. Thévenod F. Catch me if you can! Novel aspects of cadmium transport in mammalian cells. Biometals. 2010;23:857-875.
20. Champion JA, Mitragotri S. Role of target geometry in phagocytosis. Proc Natl Acad Sci U S A. 2006;103:4930-4934.
21. Ferrari E, Monzani E, Guttà C, et al. Probing the structure, function, and drugability of intermediate species in amyloid formation. J Med Chem. 2020;63:1100-1123.
22. Spillantini MG, Schmidt ML, Lee VM, et al. α-Synuclein in Lewy bodies. Nature. 1997;388:839-840.
23. Laemmli UK. Cleavage of structural proteins during the assembly of the head of bacteriophage T4. Nature. 1970;227:680-685.
24. Udenfriend S, Stein S, Böhlen P, et al. Fluorescamine: a reagent for assay of amino acids, peptides, proteins, and primary amines in the picomole range. Science. 1972;178:871-872.
25. Hare D.J, Double K.L. Iron and dopamine: a toxic couple. Brain. 2016;139:1026-1035.
26. Lees A.J, Hardy J, Revesz T. Parkinson's disease. Lancet. 2009;373:2055-2066.
27. Wright J.A, Wang X, Brown D.R. Unique copper-induced oligomers mediate α-synuclein toxicity. FASEB J. 2009;23:2384-2393.
28. Park J, Kim D.S, Park S.J, et al. A multifunctional nanoparticle system combines sonodynamic therapy and dietary restriction to colon cancer treatment. Angew Chem Int Ed Engl. 2019;58:13821-13825.
29. Kessler J.C, Rochet J.C, Lansbury P.T. Jr. The N-terminal repeat domain of α-synuclein inhibits β-sheet and amyloid fibril formation. Biochemistry. 2003;42:672-678.
30. Cremades N, Dobson C.M. The contribution of biophysical and structural studies of protein self-assembly to the design of therapeutic strategies for amyloid diseases. Neurobiol Dis. 2018;109:178-190.
31. Invited Speakers' Session. Rinsho Shinkeigaku. 2021;61:S1-220.
32. Parkinson's Disease - Animal Models, Current Therapies and Clinical Trials. IntechOpen eBooks. 2023.
33. Vincent B, Béringue V. Prion 2022 Conference abstracts: pushing the boundaries. Prion. 2022;16:95-253.
34. Merchant KM, Cedarbaum JM, Brundin P, et al. A Proposed Roadmap for Parkinson's Disease Proof of Concept Clinical Trials Investigating Compounds Targeting Alpha-Synuclein. Journal of Parkinson's Disease. 2019;9:31-61.