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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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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.

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PROGRESS IN T-CELL IMMUNE RESEARCH ON HYPERLIPIDEMIC PANCREATITIS

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Abstract.

T cells play a significant role in the immune response of hyperlipidemic pancreatitis, with their function affected by dysregulated lipid metabolism. In acute pancreatitis, rapid T-cell activation and Th2 differentiation correlate with disease severity, involving CD4+ T cells in inflammation and IL-6 in systemic T-cell activation. Chronic pancreatitis features regulatory T-cell responses and increased central memory T cells. Hyperlipidemia exacerbates pancreatic inflammation via mechanisms like ferroptosis and fatty acid-induced acinar cell pyroptosis. T-cell-targeted immunotherapies show promise, though challenges remain. Other immune cells (e.g., macrophages), environmental factors, and calcium signaling also influence the disease.

Key words. Hyperlipidemic pancreatitis, T cells, immune response, lipid metabolism, inflammation.

Introduction.

T cells play a significant role in the immune response associated with hyperlipidemic pancreatitis [1]. Hyperlipidemic pancreatitis, a condition increasingly prevalent, is linked to dysregulated lipid metabolism, which can significantly impact T-cell function [2,3]. Recent studies aim to understand how these metabolic disturbances affect T-cell differentiation, activation, and cytokine production within the context of pancreatic inflammation [4,5].

The Role of T Cells in Pancreatitis.

T lymphocytes (table 1), or T cells, are critical components of the adaptive immune system and play a vital role in various pancreatic diseases, including acute and chronic pancreatitis [1]. T cells are involved in the pathogenesis of pancreatitis, where imbalances in T-cell subsets within the pancreas contribute to disease development [1,6]. The activation of T cells following acute pancreatitis involves an antigenic effect, suggesting that T cells recognize and respond to specific antigens within the pancreas [7]. In acute pancreatitis, T cell activation is rapid, leading to T helper 2 (Th2) differentiation, which correlates with the severity of the disease8. Depletion of CD4+ T cells has been shown to improve the condition in experimental models, indicating that CD4+ T cells contribute to the inflammatory response [8].

Chronic pancreatitis is associated with disease-specific regulatory T-cell responses [9]. Studies have characterized T-cell responses against pancreatitis-associated antigens, revealing the involvement of T cells in the alternating phases of acute inflammation and quiescent disease [9]. Furthermore, an increased number of central memory T cells have been observed in patients with chronic pancreatitis, suggesting a persistent adaptive immune response [10].

Hyperlipidemia: Disrupting T-cell Subsets and Amplifying Inflammation.

Hyperlipidemia exacerbates pancreatitis by targeting T-cell subsets through metabolic reprogramming, while inducing lipid-dependent cell death pathways that further activate T-cell-mediated inflammation.

Metabolic reprogramming of T-cell subsets.

Excess lipids (e.g., free fatty acids, cholesterol) alter the metabolism of T-cell subsets, impairing their functional balance. Tregs, critical for limiting excessive inflammation, are particularly vulnerable: hyperlipidemia disrupts their mitochondrial oxidative phosphorylation, reducing Foxp3 expression and IL-10 secretion [11]. This dysfunction allows unchecked activation of proinflammatory subsets—Th1 and Th17 cells—whose secretion of IFN-γ and IL-17 amplifies pancreatic neutrophil infiltration and acinar cell necrosis [6].

$CD4^+$ T cells also undergo metabolic shifts under hyperlipidemic conditions: increased uptake of fatty acids promotes lipid droplet accumulation, enhancing their proliferation and Th2 differentiation via activation of the mTOR-HIF1α pathway [12]. This explains why hypertriglyceridemia correlates with more severe acute pancreatitis—accelerated Th2 polarization intensifies tissue damage [2]. Interleukin-6 (IL-6) has been identified as a crucial mediator of systemic T cell activation in acute pancreatitis, released by pancreatic macrophages and necrotic acinar cells [13]. IL-6 triggers systemic T cell activation, contributing to the inflammatory cascade [13].

Lipid-driven cell death and T-cell activation.

Hyperlipidemia induces ferroptosis in acinar cells—an iron-dependent process driven by lipid peroxidation—releasing damage-associated molecular patterns (DAMPs) such as HMGB1 [4,5].

Hyperlipidemia can significantly affect T cells in pancreatitis, influencing the severity and progression of the disease [14,15]. In acute pancreatitis (AP), T cell activation can initiate the development of the condition, triggering the release of cytokines associated with the Th1 response, which further exacerbates the inflammatory response [6]. Furthermore, the increasing incidence of hyperlipidemic acute pancreatitis (HLAP) highlights the clinical relevance of this interaction [2]. Studies show that hyperlipidemia can alter the function of regulatory T cells (Tregs), which are critical for maintaining self-tolerance and controlling inflammation [14]. When hyperlipidemia is induced in mice, Tregs exhibit changes that reduce their

Table 1. *Functions of T-cell Subsets in Pancreatitis and Impact of Hyperlipidemia.*

T-cell Subset	Role in Acute Pancreatitis	Role in Chronic Pancreatitis	Associated Cytokines	Impact of Hyperlipidemia
$CD4^+$ T cells	Rapid activation, drives Th2 differentiation	Sustains memory responses, promotes fibrosis	IL-4, IL-6, IL-13	Enhances proliferation and Th2 polarization via lipid uptake
Th1	Limited role, activated by DAMPs from ferroptosis	Promotes chronic inflammation via IFN-γ	IFN-γ	Accelerated differentiation via M1 macrophage cytokines
Th2	Correlates with severity, induces edema	Minimal role	IL-4, IL-13	Enhanced polarization via mTOR-HIF1α signaling
Th17	Minor role in acute phase	Drives fibrosis via IL-17	IL-17	Increased differentiation due to Treg dysfunction
Treg	Attempts to limit acute inflammation	Impaired function, fails to resolve inflammation	IL-10, TGF-β	Reduced Foxp3 expression and IL-10 secretion
Central memory T cells	Not prominent	Mediates recurrent flares, long-term antigen response	IL-2, IFN-γ	Reduced survival in smokers, accelerated activation
$CD8^+CD103^+$ T cells	Minimal role	Induces acinar cell apoptosis, promotes fibrosis	Granzyme B, perforin	Increased infiltration in hyperlipidemic-smoking cohorts

function, potentially exacerbating inflammatory responses in conditions like pancreatitis. Live-cell metabolic assays have demonstrated that hyperlipidemia alters Treg metabolism [14].

Experimental models of pancreatitis have shown rapid T cell activation and Th2 differentiation, which parallels the severity of the disease [8]. Depleting CD4+ T cells can lead to improvement, suggesting a role for these cells in the pathogenesis of pancreatitis [8]. In chronic pancreatitis, CD8+CD103+ T cells, similar to those found in intestinal intraepithelial lymphocytes, infiltrate the pancreas [12]. This infiltration suggests a potential role for these T cells in the chronic inflammatory process [12]. Disease-specific regulatory T-cell responses are also associated with chronic pancreatitis [9].

Lipid metabolism plays a significant role in T cell signaling and function [16]. Dysregulation of lipid metabolism is observed in the tumor microenvironment, where tumor cells utilize lipids for proliferation, survival, and evasion of immune surveillance [17]. Excess lipids in the tumor microenvironment can impede CD8+ T-cell activities, which is relevant in the context of pancreatic cancer as well [17]. Moreover, a lipid challenge can negatively affect autophagy, inhibiting T cell responses [11]. Pro-resolving lipid mediators can regulate T-cell immune responses, influencing the balance between inflammation and resolution [18].

In acute pancreatitis, abnormal activation of ferroptosis, a form of regulated cell death characterized by iron-dependent lipid peroxidation, can worsen the severity of the condition [5]. The relationship between BMI and acute pancreatitis, mediated by lipid metabolism, increases the risk of complications and mortality [19]. Studies using single-sample Gene Set Enrichment Analysis (ssGSEA) have compared the expression levels of immune cell-related markers in normal versus pancreatitis conditions, and non-obese versus obese groups, providing insights into how obesity and pancreatitis affect immune cell activity [19].

Interactions with Other Immune Cells: Modulating T-cell Responses.

Other immune cells act as critical intermediaries between hyperlipidemia and T-cell dysfunction, shaping the inflammatory microenvironment.

Tumor-derived extracellular vesicles (tEVs) can induce senescence and suppression in T cells through lipid metabolism reprogramming [20]. Programmed death ligand 1 (PD-L1), a key component of tEVs, plays a role in this process [20]. The study of lipid metabolism in tumor-infiltrating T cells is essential for understanding immune responses against cancer cells [21]. While mild to moderate elevations of serum triglyceride levels may be a consequence of pancreatic disease, marked hyperchylomicronemia and hypertriglyceridemia can trigger acute pancreatitis, suggesting a pre-existing defect in lipid catabolism and clearance [22]. Some studies indicate that hyperlipidemia induced by a cholesterol-rich diet can aggravate necrotizing pancreatitis [22]. Hyperlipidemia can intensify cerulein-induced acute pancreatitis, potentially associated with the activation of protein kinase C [23].

Other Immune Cells and Environmental Modulators.

Macrophages act as key intermediaries between hyperlipidemia and T-cell responses. M1 polarization, induced by excess fatty acids, drives both acinar cell pyroptosis and T-cell activation [24,25], while M2 macrophages may counteract this via anti-inflammatory cytokines (e.g., IL-10), highlighting a macrophage-Treg crosstalk that could be therapeutically targeted [4].

Environmental Factors: Influencing T-cell Subset Dynamics.

Environmental factors, such as alcohol and smoking, can modulate adaptive immunity in pancreatitis [23]. These factors can influence the overall decrease in peripheral lymphocyte counts and increase the risk of pancreatitis by differentially influencing the adaptive immune system [23]. The immunological reactivity of patients with acute pancreatitis varies depending on its genesis, with biliary pancreatitis showing increased immunological reactivity and alcoholic pancreatitis showing reduced activity.

Calcium Signaling: A Regulator of T-cell Activation and Function.

Calcium signaling is a conserved pathway linking pancreatic physiology to T-cell immunity, with dysregulation exacerbating T-cell-mediated inflammation.

In T cells, calcium influx through CRAC channels is critical for activation. Upon T-cell receptor (TCR) engagement, calcium-

dependent activation of NFAT transcription factors drives expression of IL-2, IFN-γ, and other cytokines, promoting T-cell proliferation and differentiation [26]. In hyperlipidemic conditions, excess lipids (e.g., sphingosine-1-phosphate) disrupt CRAC channel function, enhancing calcium influx and hyperactivating $CD4^+$ T cells—leading to excessive Th1/Th17 differentiation [27].

In pancreatic acinar cells, dysregulated calcium signaling triggers enzyme activation and necrosis, releasing DAMPs that activate T cells [28]. This creates a reciprocal loop: acinar cell calcium dysregulation activates T cells, while T-cell-derived cytokines (e.g., IL-6) further perturb acinar cell calcium homeostasis, amplifying inflammation. Targeting calcium signaling could thus modulate both T-cell activation and pancreatic cell damage, representing a dual therapeutic opportunity.

Calcium signaling is a unifying regulator of pancreatic physiology and pathology [29]. Dysregulated calcium fluxes in acinar cells trigger enzyme activation and cell death, releasing DAMPs that activate T cells. Additionally, calcium-dependent pathways in T cells modulate their activation and cytokine secretion, linking cellular physiology to immune responses [29].

Immunotherapeutic Targets and Future Directions.

Given the significant role of T cells in pancreatitis, immunotherapeutic strategies targeting T cells have emerged as promising avenues for treatment [30]. The dysregulation of immune cells in severe acute pancreatitis has been revealed through single-cell RNA sequencing, offering insights into potential biological markers for predicting the severity of acute pancreatitis [31]. Integration of immune cell signatures and diagnostic gene markers is crucial for identifying therapeutic targets and improving predictive diagnosis in pancreatitis [32]. T cell-based cancer immunotherapy has seen remarkable progress, driven by a deeper understanding of T cell biology and innovative screening technologies, which may offer insights applicable to pancreatitis treatment [28,33].

However, challenges remain, including the need to better understand the specific mechanisms by which T cells contribute to pancreatic inflammation and to develop targeted therapies that can modulate T-cell responses without causing systemic immunosuppression [23,34]. The role of hypoxia in CD8+ T cell localization and function in pancreatic cancer highlights the importance of understanding the microenvironment in modulating immune cell activity, which could be relevant in pancreatitis as well [35].

Conclusion.

Hyperlipidemic pancreatitis arises from a dynamic interplay between lipid metabolism dysregulation and T-cell-mediated immunity. Hyperlipidemia disrupts Treg function, promotes ferroptosis and pyroptosis, and primes proinflammatory T-cell subsets-all amplified by macrophage crosstalk. Future research must clarify subset-specific T-cell mechanisms (e.g., $CD4^+$ Th2 vs. $CD8^+$ cytotoxic T cells) and environmental modifiers to develop targeted therapies. By integrating lipid metabolism, cell death, and immune cell dynamics, we can advance our understanding of this complex disease and improve patient outcomes.

Data availability.

All data are contained in the article. The raw data will be shared upon request. Contact the corresponding author.

Consent for publication.

All authors have agreed to the publication of this paper.

Competing interests.

The authors declare no competing interests.

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