ACCSCIENCE PUBLISHING

Cancer Plus

ORIGINAL RESEARCH ARTICLE

MXene-montmorillonite nanocomposites-based scaffold sensors for early pancreatic cancer diagnosis

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Abstract

Pancreatic cancer is increasingly prevalent and characterized by a high mortality rate. Due to the limitations of current diagnostic methods, early-stage detection remains elusive, contributing to persistently low survival rates among affected individuals. Nanomaterials have garnered significant attention in cancer research for their potential diagnostic applications. Among these, MXenes – a novel family of two-dimensional nanomaterials composed of transition metal carbides, nitrides, and carbonitrides – are of particular interest due to their unique properties. These include high electrical conductivity, hydrophilicity, thermal stability, large interlayer spacing, tunable structure, and high surface area. These characteristics make MXenes highly effective for detecting trace amounts of various analytes. In addition, their tunable structure enables precise manipulation of their properties, allowing for optimized sensing responses. Montmorillonite nanoclay (MMT), a member of the smectite group of natural clay minerals, is known for its ability to promote bone development and influence cell behavior. When combined with MXenes, MMT forms promising nanocomposites for early pancreatic cancer detection through sensing applications. The Ti_3C_2 MXene-MMT nanocomposites exhibit potential as scaffold sensors capable of distinguishing cancerous from non-cancerous samples by observing the distinctive patterns in resistance changes. In addition, MXenes possess excellent selectivity, allowing for the reliable identification of targeted analytes from a complex mixture of chemical and biological analytes. Due to the advanced sensing capabilities of MXene-MMT composite scaffold sensors, they hold great promise for early cancer diagnosis and tissue regeneration, providing a novel therapeutic approach to improving patient outcomes.

Keywords: Sensor; Scaffold; MXene; Nanocomposite; Nanoclay; Nanomaterial

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Citation: Sadiq M, Hoang Q, Kishlock A, *et al.* MXene-montmorillonite nanocomposites-based scaffold sensors for early pancreatic cancer diagnosis. *Cancer Plus*. 2024;6(3):3793. doi: 10.36922/cp.3793

Received: May 30, 2024

Accepted: August 28, 2024

Published Online: October 9, 2024

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1. Introduction

Pancreatic cancer, a highly fatal malignancy, has become one of the most tenacious adversaries in modern oncology. At present, there is no widely accepted standard screening program for pancreatic cancer in the general population, primarily due to the challenging nature of detecting the disease at an early stage. The majority of cases are diagnosed when the cancer has already progressed to an advanced stage, contributing to a poor prognosis. This issue is compounded by the fact that many individuals with pancreatic cancer often do not experience noticeable symptoms until the disease has significantly advanced. As a result, the absence of early symptoms, combined with the aggressive nature of the disease, makes routine screening for the general population difficult to implement. Pancreatic cancer can develop from exocrine cells and neuroendocrine cells, namely islet cells. The more prevalent exocrine form is typically diagnosed at an advanced stage, whereas islet cell tumors, a rarer subtype of pancreatic neuroendocrine tumors, often have a more favorable prognosis. Symptoms of pancreatic cancer include jaundice (yellowing of the skin and eyes), back and abdominal pain, fatigue, and unintentional weight loss. Detecting pancreatic tumors during routine physical examinations is challenging due to the pancreas's deep location in the abdomen and its tendency to be obscured in imaging. The combination of late detection and the rapid progression of the disease often renders pancreatic cancer incurable at the time of diagnosis. Consequently, its 5-year survival rate remains alarmingly low, and the number of cancer-related deaths from pancreatic cancer continues to rise.[1] Thus, early detection, along with the development of innovative diagnostic tools and advanced therapeutic strategies, is essential for improving outcomes in patients with pancreatic cancer.

In recent years, significant research efforts have been directed toward detecting pancreatic cancer at earlier stages. Current advances in oncology are increasingly focused on the development of functional nanomaterials with improved diagnostic accuracy. One promising technology in this realm is the use of chemiresistive sensors. These sensors belong to a class of chemical sensors that measure changes in electrical resistance when the sensing material interacts with a specific analyte.

Chemiresistive sensors provide valuable information about the composition of a system in real time. This is achieved by coupling a chemically selective layer, known as the recognition element, with a chemical transducer. The basic structure of the sensor includes a sensing material and a set of electrodes. The sensing material either bridges the gap between electrodes or coats a set of interdigitated electrodes. Upon exposure to target analytes, chemical interactions with the sensing material lead to measurable changes in electrical resistance.

The real-time resistance changes recorded by chemiresistive sensors offer critical insights into the presence and concentration of specific analytes, making them highly effective for detecting biomarkers associated with pancreatic cancer. Given the aggressive nature of pancreatic cancer and the urgent need for early diagnosis, advancements in chemiresistive sensor design hold great potential for improving treatment outcomes. By advancing the design and functionality of these sensors, researchers aim to develop more sensitive and selective diagnostic tools capable of detecting pancreatic cancer at its earliest and most treatable stages.

Our current research focuses on exploring the potential of using a novel functional two-dimensional (2D) nanomaterial, MXene, in chemiresistive sensors for early-stage pancreatic detection. Preliminary results indicate that MXene-based chemiresistive sensors can detect cancer cells even at extremely low concentrations. MXenes are a group of 2D transition metal carbides, nitrides, and carbonitrides with the general formula $M_{n+1}X_nT_x$ (n represents 1, 2, or 3; M represents transition metal: Ti, V, Nb, Mo; X represents C and/or N; and T represents surface terminations such as -OH, -F, or =O). These materials are synthesized by selectively etching parent ternary carbide MAX compounds, removing the A-group member (e.g., converting layered MAX phase Ti_3AlC_2 to Ti_3C_2 to create MXenes). Although several investigations have concentrated on single-layer MXene, they are often produced as thin films consisting of multiple MXene flakes with wide interlayer spacing, held together by weak Van der Waals forces. Due to this unique fabrication mechanism, MXenes, unlike other 2D materials, exhibit a desirable combination of high electronic conductivity, hydrophilicity, and chemical stability. In addition to these characteristics, MXenes possess a large specific surface area (250 – 1000 m^2), further enhancing their sensing capabilities. These unique material properties make MXenes highly effective for early-stage disease detection, offering a promising avenue for enhancing pancreatic cancer diagnostics.

1.1. Electrical properties of MXene

MXenes exhibit semiconducting or semimetallic properties, depending on their electronic structure, which is intricately tied to their elemental composition. The characteristics of the M element (transition metal), X element (carbon or nitrogen), and surface terminations profoundly impact the electronic properties of MXenes.[2] The electronic structure, closely linked to their composition and organization, plays a crucial role in determining key properties such as electrical conductivity and charge storage capabilities.

The unique configuration of transition metal carbide or nitride layers, along with various surface functional groups, significantly contributes to the electronic characteristics of MXenes. These characteristics include bandgap, electron affinity, and overall conductivity. The interplay between the M and X elements forms a framework that supports high electrical conductivity and efficient charge storage and transfer.

Surface terminations, which can include groups such as hydroxyls, oxygen, or fluorine, further modify the electronic properties of MXenes. These surface groups influence the distribution of electron density and the potential energy landscape, thereby affecting electron mobility within the material. This tunability allows for the customization of MXenes for specific applications, such as sensors, energy storage devices, and catalysts.

Understanding and manipulating the electronic structure of MXenes through elemental composition and surface modification opens up a wide range of possibilities for designing materials with tailored electronic properties. This potential makes MXenes highly versatile and promising for advanced technological applications where precise control over electronic properties is crucial.

Various factors, such as terminal groups,[3] interlamellar spacing, and ambient temperature,[4] commonly affect the electrical conductivity of MXenes. For instance, some MXenes can transition from metallic to semiconducting properties depending on their surface functional groups. Synthesis processes, including etching and delamination, can further control the electronic and electrical properties of MXenes. For example, the electrical conductivity of $Ti_3C_2T_x$ can be significantly enhanced by eliminating a portion of surface functional groups through annealing in a vacuum.[5] High conductivity can also be achieved by ensuring precise contact between individual flakes and using intercalants to increase interlayer spacing, thereby reducing resistivity.

In a study by Muckley *et al.*,[6] the intercalation of H_2O and Li^+ into $Ti_3C_2T_x$ resulted in a decrease in resistance from 41 Ω to 10 Ω. Temperature also influences the electron conductivity of $Ti_3C_2T_x$ MXene. Studies by Halim *et al.*[7] and Bergmann[8] showed that the resistivity of 2D $Ti_3C_2T_x$ nanofilms increased from 4.8 to 6.1 μΩ·m as the temperature dropped below 100 K, a change attributed to electron backscattering – a phenomenon commonly observed in 2D metallic materials.

The conductivity of MXenes can be further enhanced by optimizing flake-to-flake contact and using intercalants to increase interlayer spacing. Under specific delamination and etching conditions, MXenes can achieve conductivities ranging from 10,000 to over 6500 S cm-1, surpassing graphene in conductivity.[9] In addition, MXenes featuring hydrophilic surfaces terminated with hydroxyl groups and conductive 2D carbide layers exhibit enhanced capacitances exceeding 300 F/cm^3 through electrochemical intercalation with various cations. This capacitance greatly surpasses that of porous carbons.[10] When used as electrodes, MXenes facilitate efficient electron flow with minimal resistance, contributing to improved energy efficiency and reduced power requirements in devices.[11]

1.2. Application to cancer theranostics

Precision control over functional groups allows for the customization of MXene surface chemistry, paving the way for extensive innovation. By deliberately modifying surface terminations,[12] scientists can engineer MXene-based materials with specific properties, fine-tuning them for catalytic reactions, creating highly responsive sensors for diverse analytes, and advancing the development of sophisticated biomedical devices. The following desirable characteristics make MXenes particularly suitable for cancer detection or treatment when compared to other nanomaterials:

(i) The hydrophilic character of MXenes, due to functional groups such as -OH, -O, or -F introduced during the etching process, offers significant potential for surface modification. This negatively charged surface enhances selective and efficient interactions with cancer cells[13,14]
(ii) MXenes' large surface/interface area facilitates molecular absorption/desorption between the material and analytes, thereby improving sensitivity. Their substantial surface area, metallic conductivity, and adjustable functionalization make MXenes effective transducers. When functionalized with precise biological receptors, they enable electrochemical sensing of various biomolecules with high specificity[15]
(iii) Studies have proven that MXenes are non-toxic and biocompatible with living organisms.[16,17] This biocompatibility may be due to the relative inertness of the metals in the M layer of MXene, such as Ti, Mo, and Nb, as well as the essential role of elements, such as nitrogen and carbon, in biological systems.[16-18] The ability of MXenes to degrade and be eliminated from the bodies of mice provides direct evidence of their biosafety and biocompatibility.[19]

1.3. MXene-nanocomposite

The sensitivity of MXenes can be further improved by compositing them with other nanomaterials. Nanoclays, such as montmorillonite (MMT), are biocompatible and encourage osteogenic cell behavior, such as adhesion, proliferation, spreading, and differentiation.[20] MMT is composed of phyllosilicate minerals with a nanolayered structure. Each layer, approximately 1 nm thick, consists of two O-Si-O tetrahedral sheets sandwiching an O-Al (or Mg)-O octahedral sheet (Mt).[21] Silicon ions, surrounded by hydroxyl atoms at the axial end of the tetrahedral planes, replace aluminum ions on the octahedral subunits, imparting a slight negative charge. MMT nanoclay is naturally hydrophilic and capable of forming electrostatic and hydrogen bonds with other materials. It promotes major bone defect repair and is biodegradable.[20,22] In this context, MXene serves as the host sensing material for cancer detection, whereas MMT acts as a scaffold material for tissue regeneration. In the present study, we developed a scaffold sensor based on MXene-MMT nanocomposites for detecting pancreatic cancer and supporting tissue regeneration.

2. Materials and methods

The preparation methods for MXene and Mxene-MMT nanomaterial slides for testing with various samples to detect the presence of pancreatic cancer are described in this section.

2.1. Preparation of MXene

To synthesize the MAX phase Ti_3AlC_2, TiC, Ti, and Al powders (MSE Supplies®, USA) were initially ball-milled for 2 h. The resulting powder mixture was pressed into pellets and sintered at 1350°C for 4 h under an argon atmosphere. After sintering, the pellets were milled back into powder form and sieved using a 160-mesh sieve. The collected MAX phase powder was stored in a glass vial for further use.

In situ hydrogen fluoride (HF) was prepared using fluoride-based salt etchants (Sigma-Aldrich, USA), as shown in Figure 1. Specifically, 15 mL of hydrochloric acid (HCl) (99.9%, Sigma-Aldrich, USA) and 5 mL of deionized water were mixed with 1.6 g of lithium fluoride (LiF) (Sigma-Aldrich, USA), and the mixture was stirred continuously for 5 min. Following this, 1.0 g of Ti_3AlC_2 powder was gradually added to the etchant solution, allowing the reaction to proceed for 48 h at room temperature.

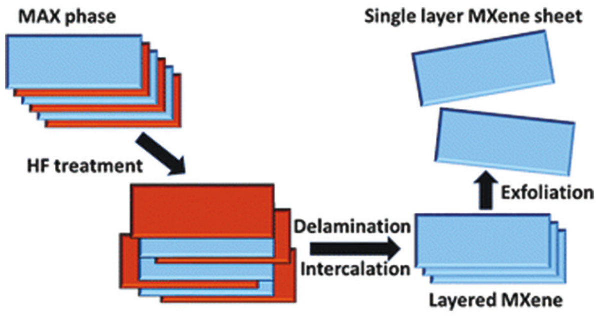

Figure 1. Preparation of MXene from MAX phase. Reproduced with permission from Shukla[23]
Abbreviation: HF: Hydrogen fluoride.

2.2. Mild hydrothermal process

The etchants, including LiF, HCl, and MAX, were initially weighed out in the same stoichiometric ratio as for the *in situ* HF preparation. The mixture was stirred at room temperature for an hour in a Teflon bottle. The resulting solution was then placed in an autoclave and processed in a tube furnace for 48 h at varying temperatures of 30°C, 60°C, and 80°C to produce three distinct MXene samples. After 48 h, the etching process for each sample was completed.

The washing procedure involved centrifuging the acidic mixtures at 6,000 rpm for 5 min, repeating the cycle several times until the pH of the solution reached 4 – 5. Once washing was complete, the black slurry of $Ti_3C_2T_x$ was carefully separated from the remaining $Ti_3AlC_2/Ti_3C_2T_x$ residue using a spatula. The synthesized MXene displayed a unique accordion-like morphology (Figure 2).

2.3. Preparation of MXene-MMT nanocomposite

First, MXene and MMT powders were weighed in a 2:1 mass ratio. Each type of powder was ground separately using a mortar for 30 minutes. The ground MXene was transferred into one glass vial, and the ground MMT powder into another. Ethanol was added to each vial to create a paste, and the dispersions were stirred for 1 – 2 h until a uniform paste was formed. Once the paste

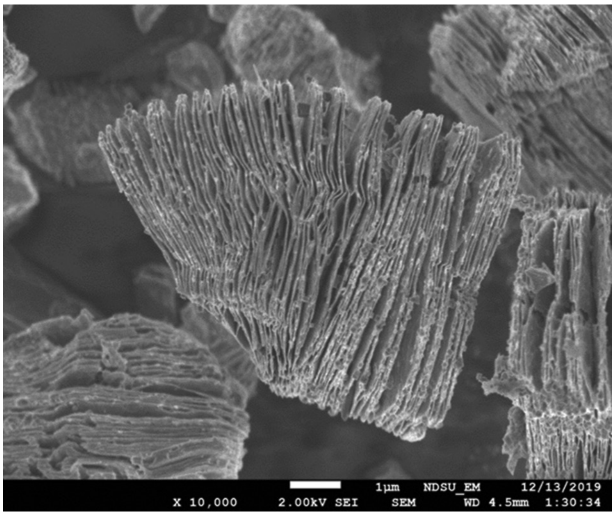

Figure 2. Scanning electron microscopic image of pure MXene. Scale bar: 1 μm; magnification: ×10,000

was ready, five drops of MMT paste were added to the MXene vial using a dropper, and the mixture was stirred for an additional hour. After stirring, the MXene and MMT nanocomposite paste (Figure 3) was ready and was uniformly coated onto interdigitated gold electrode glass slides. The coated nanocomposite glass slides were dried in a vacuum oven at 50°C overnight. In our work, we used MMT that had been modified with 5-aminovaleric acid.[24] The reasons for using modified MMT instead of untreated MMT are explained in detail in the results section.

The Mxene and MXene-MMT nanocomposite slides were tested with protein samples extracted from human pancreatic cancer cell lines (MIA PaCa-2) and human pancreatic epithelial cell lines (HPNE).

The human pancreas cell lines HPNE, and MIA PaCa-2 were obtained from the American Type Culture Collection (ATCC, USA). MIA PaCa-2, and HPNE cells were cultured in DMEM media (Hyclone, GE Healthcare Life Sciences, USA). The DMEM medium used for HPNE cells was supplemented with 0.1 ng/mL epidermal growth factor (Novus Biologicals, USA). Penicillin and 10% fetal bovine serum (FBS; Life Technologies, Thermo Scientific Inc., USA) were added to all cultures as supplements (1 U). The cells were maintained at 37°C in a humidified incubator with 5% CO_2.

2.4. Protein extraction

The cells were allowed to grow in a petri dish until they reached 85 – 95% confluency. After the medium was removed from the plate, the cells were washed twice with phosphate-buffered saline before adding 1 mL of lysis buffer. The cells were incubated for 30 min at 4°C. Following the incubation, the lysed cells were collected and centrifuged twice to obtain pure protein samples. Since our sensor operates on a chemiresistive principle, resistance was monitored for up to 48 h for each slide with the samples. Distinct patterns were observed for different slides and samples, which will be further analyzed in the results section.

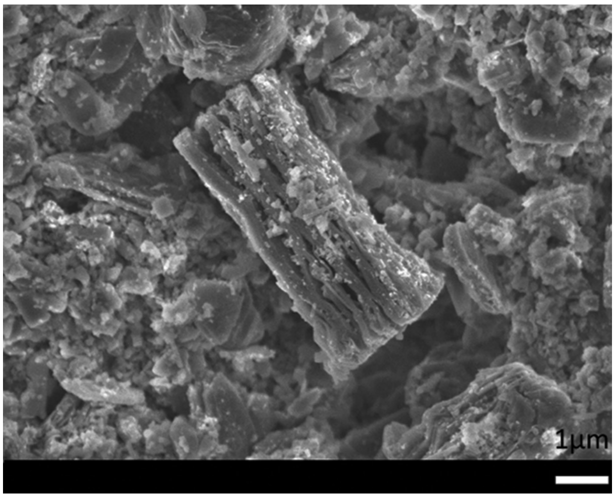

Figure 3. Scanning electron microscopic image of MXene-MMT composite. Scale bar: 1 μm; magnification: ×10,000

3. Results and discussion

3.1. Evaluation of pure MXene at 30°C

The results of the evaluation of pure MXene at 30°C are illustrated in Figure 4 and discussed in detail in the following subsections.

3.1.1. Proteins from MIA cell lines (cancerous) on pure MXene slides

After the application of the protein samples, the resistance of the pure MXene slides did not significantly alter for the first 2 h. The resistance peaked during the 2nd h, then declined rapidly until the 6th h, after which it remained stable until the data collection was complete at the 48th h.

3.1.2. Proteins from HPNE cell lines (healthy) on pure MXene slides

For the pure MXene slides treated with HPNE-derived proteins, the resistance increased slightly during the 2nd hour, followed by a gradual decline, showing a trend similar to that observed with the MIA cell lines. Overall, the resistance change was minimal, and the trend was considered stable.

3.2. Evaluation of MXene-MMT nanocomposite at 30°C

The results of the evaluation of MXene-MMT nanocomposite at 30°C are illustrated in Figure 5 and discussed in detail in the following subsections.

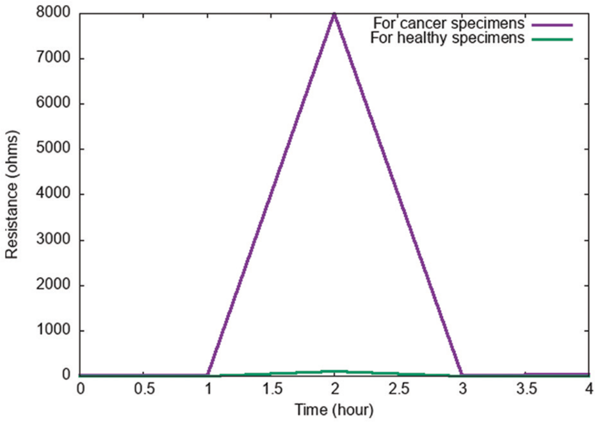

Figure 4. Resistance change of pure MXene upon administration of proteins from MIA and HPNE cell lines

3.2.1. Proteins from MIA cell lines (cancerous) on MXene-MMT slides

For the MXene-MMT nanocomposite slides treated with proteins from the MIA cell lines, the resistance increased immediately and rapidly until the 2nd h. Afterward, the resistance decreased slightly until the 6th h, after which it began to drop more rapidly until the 24th h. From that point onward, the resistance decreased gradually until the 48th h, where it remained steady.

3.2.2. Proteins from HPNE cell lines (healthy) on MXene-MMT slides

For the MXene-MMT nanocomposite slides treated with proteins from healthy HPNE cell lines, resistance increased rapidly until the 2nd h, then dropped significantly, mirroring the pattern observed in the MIA cell line slides. The resistance remained steady after the 6th h.

3.3. Evaluation of MIA cell-derived proteins with MXene-MMT (untreated and treated) nanocomposite at 60℃

The curve in Figure 6 reveals the preference for the MXene-MMT composite treated with 5-aminovaleric acid over untreated MXene-MMT. It was discovered that the modified MMT slide, when combined with MXene, was more sensitive and exhibited a larger change resistance, making it more dependable for our research purposes. This conclusion was drawn from testing both slides with protein derived from MIA cell lines.

3.4. Sensing scheme for protein

MXenes are characterized by a 2D layered, graphene-like morphology. Unlike other 2D materials, MXenes exhibit a higher response with a strong signal-to-noise ratio due to the robust binding of functional groups with analytes.[14] This strong binding increases the relative intensity of the analyte signal in comparison to background noise. The near-free electron states at the Fermi level in MXene structures facilitate rapid charge-carrier transport along electron transport channels.[25] Combined with their metallic conductivity and numerous surface functional groups that form strong connections with analytes, these properties significantly contribute to MXenes' exceptional sensing abilities.[26]

The sensing mechanism in MXene structures differs from that of metal oxides and is more complex than simple surface adsorption or charge transfer observed in typical 2D materials.[27] For sensors based on metal oxides, the sensing mechanism relies on surface reactions of analyte molecules with pre-adsorbed oxygen species. In contrast, the sensing mechanism of MXene materials is driven by charge transfer resulting from the physisorption of analyte molecules on the surface, without the involvement of adsorbed oxygen species. Consequently, changes in electrical characteristics are governed by the adsorption/desorption process.[28]

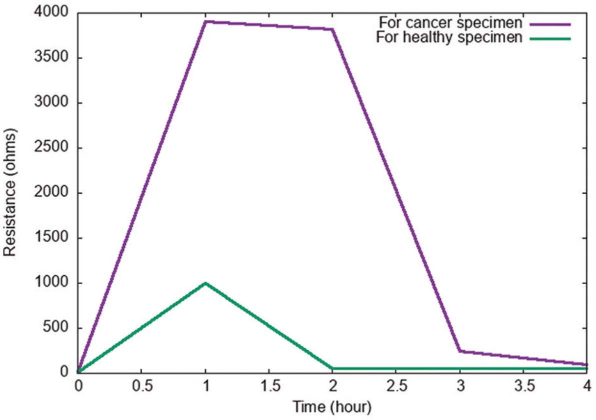

Figure 5. Resistance change of MXene-MMT nanocomposite upon administration of proteins from MIA and HPNE cell lines

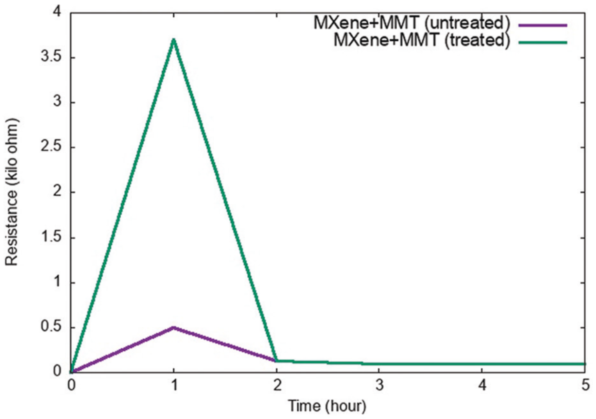

Figure 6. Comparison of the resistance change of untreated MXene-MMT and MXene-MMT treated with 5-aminovaleric acid, tested with protein derived from MIA cell lines

Due to their metallic-like conductivity, MXenes exhibit increased resistance when detecting both oxidizing and reducing agents. Analyte adsorption is influenced by charge transfer within $Ti_3C_2T_x$-based sensitive layers, a behavior linked to the rapid electron transfer and mobility within the MXene structure. Furthermore, the construction of composites or hybrid structures can modify the sensing process, as additional compounds can act as "catalysts" to enhance the sensing capabilities of the base material.[29]

Overall, MXenes' exceptional sensing abilities are attributed to their 2D layered structure, rapid charge-carrier transport, strong binding with analytes, and metallic conductivity. These properties give MXenes significant advantages over traditional 2D materials and metal oxides, making them highly effective for various sensing applications. The incorporation of other compounds to form composites further enhances these capabilities, positioning MXenes as a promising material for advanced sensor technologies.

MXene materials also possess a unique layered structure that distinguishes them in advanced material science. This structure consists of layers of transition metal carbides or nitrides interspersed with intercalated species. The spacing between these layers is crucial for ion intercalation and deintercalation processes, particularly vital for energy storage applications. For high-quality MXenes, intercalation often becomes an additional, if not essential, step that significantly influences their properties. Typically, MXenes have a negatively charged surface due to their 2D layered structure, allowing them to accommodate various mono- and multivalent cations, polar organic molecules, and nanoparticles within their interlayer space.[30] In addition, nanowires, nanosheets, and other layered materials can be encapsulated within the space between MXene layers, which can also be filled with polymers to create hybrid structures.

The interlayer distance, which significantly affects MXenes' behavior, can be expanded due to the presence of intercalants occupying the interlayer space or the need for electrostatic balance. Controlling this interlayer distance presents an opportunity to enhance various performance characteristics. However, limited knowledge about the confinement and filling mechanisms hinders a complete understanding of the interactions that cause structural and chemical changes within the MXene interlayers. Gaining this insight is crucial for effectively functionalizing the interlayer fillings.

MXenes' ability to host intercalants and modify their interlayer spacing is especially effective in fields such as energy storage, heterogeneous catalysis, and ion/electronic transport. These properties position MXenes as a promising material for advanced technological applications, where controlling interlayer interactions can lead to significant performance improvements.[31]

Although both MXenes and MMT nanoclay are negatively charged, MXenes exhibit a higher cation exchange capability, which allows them to polarize the core of the comparatively weakly charged MMT nanoclay. This polarization results in a slight positive charge on one side of the MMT nanoclay and a slight negative charge on the other. As a result, despite their identical overall charge, the two nanomaterials form a nanocomposite. The MMT nanoclay, confined between the MXene layers, prevents the restacking of the MXene layers, expanding their interlayer space, increasing active sites, and shortening the ion diffusion path, ultimately enhancing analyte interaction.

Proteins, which are polypeptides with well-defined structures, carry a net surface charge that depends on the pH of their surrounding medium. Their adsorption onto the active surface of nanoparticles is facilitated by various forces, including hydrogen bonds, solvation forces, and Van der Waals interactions.[32] The formation of nanoparticle-protein complexes is a multifactorial process influenced not only by the characteristics of both the nanoparticles but also by the interacting proteins and the surrounding medium. The specific association and dissociation rates of each protein determine the duration of their interaction with the nanoparticle surface. Irreversible or long-term binding of proteins to the nanoparticle results in the formation of a "hard corona," whereas rapid, reversible binding of proteins with faster exchange rates leads to the formation of a "soft corona."[33]

Due to the negative surface charge of MXene and MXene-MMT nanoclay, protein adsorption induces a rapid charge transfer and diffusion in the sensing materials. Both MXene and MXene-MMT exhibit a significantly higher response to cancer cells compared to healthy cells. This higher response is due to the fact that metabolically active cancer cells have a negatively charged surface.[34] In addition, the MXene-MMT-based sensor exhibits enhanced performance due to the introduction of MMT, which improves the material's biocompatibility and strengthens its interaction with cells.

4. Conclusion

Pancreatic cancer is notorious for its rapid spread and the difficulty in detecting it in its early stages. This challenge can be addressed by MXene-based nanomaterial sensors, which exhibit unique sensing characteristics that enable the ultra-sensitive and highly selective detection of pancreatic cancer at extremely early stages. The adjustable properties of these sensors allow for fine-tuning their sensitivity and reactivity, making them highly versatile. In addition, when MXenes are combined with other nanomaterials, they form nanocomposites that significantly enhance both cancer diagnosis and post-treatment efficacy.

In our research, we specifically combined MXenes with MMT to further enhance their functionality. This innovative combination has proven to be superior to MXene-based sensors alone, as it responds more swiftly to both cancerous and non-cancerous media. This rapid response is crucial for early detection and effective intervention. Furthermore, the tissue regeneration capabilities of MMT nanoclay play a vital role in repairing tissues at the surgical site following the removal of carcinogenic tissues. This dual functionality not only improves diagnostic accuracy but also supports tissue recovery, significantly enhancing the overall treatment process. Consequently, this approach holds great promise for improving treatment outcomes in pancreatic cancer.

Moreover, the biocompatibility and mechanical strength of MMT nanoclay add another layer of functionality, facilitating improved integration with biological tissues. These advantages of MMT nanoclay ensure that the scaffold sensors can operate effectively within the human body without triggering adverse reactions. Consequently, MXene-MMT nanocomposites not only advance early cancer detection but also pave the way for innovations in biomedical applications, ultimately contributing to more effective and holistic treatment strategies for pancreatic cancer treatment. These advancements highlight the potential for a transformative impact on patient care.

Acknowledgments

The authors would like to thank Dr. Dali Sun from the Department of Electrical and Computer Engineering at the University of Denver for providing the cancer cells used in this work and for valuable discussions regarding the results.

Funding

This work was supported by the National Science Foundation (Eager-2226202, RII Track 2 – 2218046, and RII-Track-1: ND-ACES 1946202), ND Economic Diversification Research Funds (ND-EDRF), and ND EPSCoR. The results, discussion, and opinions reflected in this paper are those of the authors only and do not necessarily represent those of the sponsors.

Conflict of interest

The authors declare they have no competing interests.

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Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data

Data used in this work are available from the corresponding author upon reasonable request.

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