

## REVIEW

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# SGVYKVAIDWQH: A Specific Mimotope or A Target-Unrelated Peptide?

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**Abstract:** The peptide SGVYKVAIDWQH challenges the traditional understanding of mimotopes, generally characterized by specific binding to a defined target. In contrast, this peptide exhibits a broad interaction profile, binding to various biological and non-biological targets, including proteins, small molecules, and cellular entities. This review systematically evaluates SGVYKVAIDWQH binding affinities across 22 peer-reviewed studies and 16 patents, revealing high-affinity interactions with proteins and moderate binding to non-biological targets and cells. Utilizing data from the Biopanning Data Bank and relevant bioinformatics tools (TUPDB, MimoSearch, TUPScan, and PSBinder), we analyzed the peptide's diverse interactions. Our study identified 26 distinct targets, including receptors, antigens, and small molecules, with significant binding observed to protein targets (e.g., CD133, HER2), cellular targets (e.g., blood-brain barrier, breast cancer cells), and even non-biological substances (e.g., printer toner, parabens). Despite its frequent selection across different targets, PSBinder predictions suggest a 91% likelihood that SGVYKVAIDWQH is a polystyrene surface-binding peptide. This implies that SGVYKVAIDWQH may function as a target-unrelated peptide rather than a specific mimotope. This review and comprehensive analysis reveal the peptide's promiscuous binding behavior, offering new insights into its classification and potential applications.

**Keywords:** solid waste management, recycle, in-service teachers, belief, concern, practice

## 1. Introduction

The role of peptides in recent therapeutic advancements has garnered significant attention due to their unique properties, including high binding affinity, ease of synthesis, reduced immunogenicity, and adaptability for chemical conjugation [1]. Peptides serve as effective targeting ligands in various drug delivery systems, enhancing their utility in both clinical and research settings [2, 3]. A powerful method for discovering and characterizing these peptides is the phage display technology, which allows for the systematic identification of peptides with affinity to cells, proteins, or tissues through iterative rounds of selection, a process known as Biopanning [2, 4]. Since its introduction, phage display has revolutionized the study of protein-protein interactions and remains widely accepted for its ability to identify ligands [1–4]. In the phage display process, the material used to screen the library is referred to as the target, while the natural binding molecule of the target is termed as the template. Mimotopes, first described by Geysen et al. [5], are peptides that mimic the template's binding site and interact with the target. These mimotopes can be identified by screening random peptide libraries displayed via phage. However, alongside mimotopes, biopanning often results in the selection of target-unrelated peptides (TUPs) [6–9], which can frustrate researchers by binding not to the intended target but to impurities or other

components in the screening system [7, 8]. TUPs fall into two categories: selection-related TUPs, which interact with contaminants or elements of the screening system, and propagation-related TUPs, where some phages replicate more rapidly in host cells, thus dominating the output [7–9]. Differentiating TUPs from true mimotopes is crucial for the accurate classification and utilization of peptides in research and therapeutic applications.

In response to the rapid growth of peptide discovery, several databases have been developed to organize biopanning data. Two notable examples are the Artificially Selected Proteins/Peptides Database (ASPD) [10] and the Biopanning Data Bank (BDB) [11]. While ASPD has not been updated since 2002 and contains only 195 biopanning datasets, BDB, established in 2010 (initially known as MimoDB), has grown to become the most comprehensive resource for biopanning data. The most recent update to BDB occurred in October 2023, with continuous updates essential for maintaining relevance in bioinformatics [12]. During this update, we found that the 12-mer peptide SVSVGMPKSPRP was the most frequently repeated sequence, appearing 61 times, followed by SGVYKVAIDWQH, which occurred 34 times [12]. While SVSVGMPKSPRP has been extensively studied [13], SGVYKVAIDWQH has not yet undergone a comprehensive review. Two analysis tools in the BDB database were utilized to investigate the characteristics of the peptide SGVYKVAIDWQH. The first tool, TUPScan, is a motif-based data scanning system designed to identify potential TUPs by detecting known TUP patterns [14]. The second tool, MimoSearch, is a data analysis platform used in the identification of peptides identical to the query

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peptide in the BDB database and provides relevant information [14]. Using TUPScan, no established TUP motifs were detected in SGVYKVAYDWQH, suggesting it does not conform to known TUP classifications. Meanwhile, MimoSearch linked the peptide to 34 unique biopanning datasets and 26 distinct molecular targets, providing a broad interaction profile for further analysis. The corresponding PMID references were employed to retrieve relevant publications, resulting in a final selection of 22 unique articles after excluding 12 duplicate entries. In parallel, a comprehensive search on Google Patents identified 16 patents directly related to the SGVYKVAYDWQH peptide sequence, further expanding the scope of the review [15].

The high affinity and frequent occurrence of SGVYKVAYDWQH across multiple targets make it a peptide of particular interest. Initially classified as a mimotope, its broad binding profile has raised concerns about its specificity, prompting questions about whether it may act as a TUP. Despite its extensive presence in databases and patents [12, 15], significant gaps remain in understanding its true nature. Current literature focuses on individual interactions, but a comprehensive investigation of its broad-spectrum binding behavior is lacking. Addressing this gap is critical for determining the peptide's classification and potential applications in therapeutic research.

## 2. Material and Methods

### 2.1. The methodological approach

The BDB (<http://i.uestc.edu.cn/bdb>) was accessed to accurately download the latest dataset which was efficiently updated on the 9th of January 2023 [12]. To appropriately analyze the peptide sequence, we executed a custom command to effectively extract and determine all repetitive peptide sequences within the dataset. These sequences were then further sorted by their frequency of occurrence. The SGVYKVAYDWQH peptide was ranked second with 34 repeats following the SVSVGMPKSPRP peptide which obtained 61 repeats. The latter is recognized with wide-range adhesive peptide and TUPs [13].

To successfully evaluate the potential TUP characteristics of SGVYKVAYDWQH, the peptide sequence was carefully analyzed by employing TUPScan tool (<http://i.uestc.edu.cn/bdb/index.php/site/tools?type=TUPScan>), accessible on the BDB platform. The peptide sequence was inputted into the specified field of the tool where the “Scan” function was applied. This specific analysis ensures for determining the peptide sequence as TUP motifs thereby offering an initial clue of its binding profile.

Further, a similar analysis was executed utilizing TUPScan tool on the TUPB database as per the attached link (<https://i.uestc.edu.cn/tupdb/cgi-bin/tupscan.pl>) which is uniquely specialized for TUP motifs across a larger set of sequences. It was determined that both tools did not reveal any known TUP motifs, suggesting SGVYKVAYDWQH does not exhibit similar features of the previously identified TUPs.

Furthermore, the peptide sequence was equally subjected to a MimoSearch analysis on the BDB platform using the provided link (<https://i.uestc.edu.cn/bdb/index.php/site/tools?type=MimoSearch>). This tool is efficient in identifying peptides acting as mimotopes by appropriately matching the given sequence to known targets within the BDB dataset. Upon performing the search, it revealed that 34 distinct Biopanning dataset IDs corresponding to 26 unique targets were identified. This analysis offers significant insights on the potential of the

peptide acting as a mimotope by demonstrating its binding ability to varied biological and non-biological targets.

Finally, to effectively assess the peptide's potential as a polystyrene surface-binding peptide (PSBP), the PSBinder tool from the SAROTUP tool suite (<https://i.uestc.edu.cn/sarotup3/cgi-bin/PSBinder.pl>) was applied. The input involving the sequence of the peptide was performed using the PSBinder tool and the “Predict” function to effectively evaluate the affinity of the peptide for binding to polystyrene surfaces. Essentially, for all the analysis performed, default settings were utilized unless otherwise specified, in order to ensure consistent assessment of the parameters across different tools.

### 2.2. Thresholds and parameters

The application of the Bioinformatics tool in the analysis employed default threshold and parameters in order to appropriately maintain consistency across analyses. Specifically,

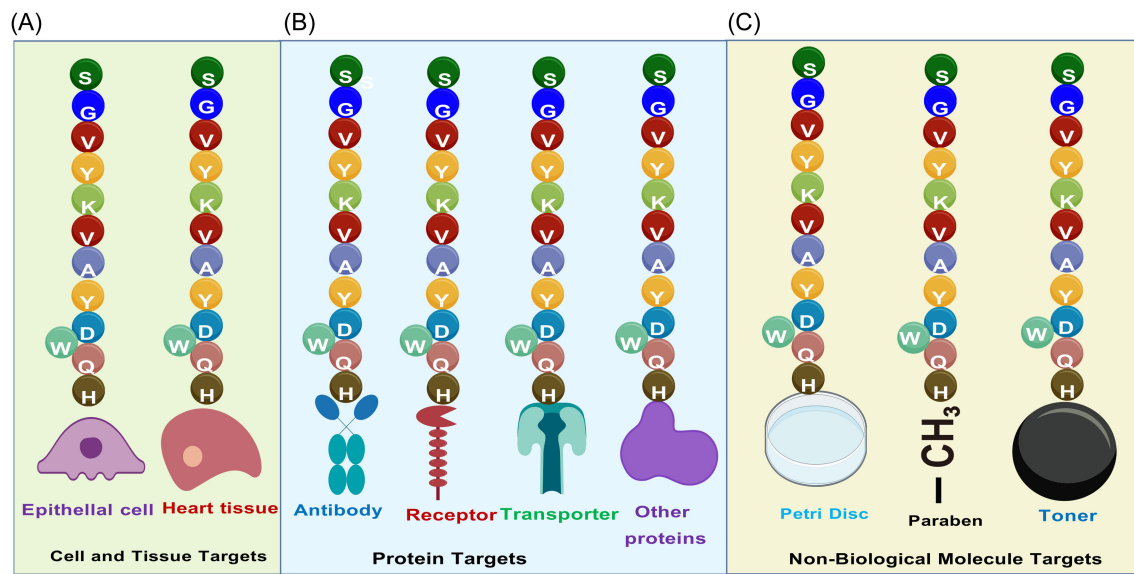
TUPScan and TUPDB employed default settings to effectively scan for known TUP motifs and cross-reference with the wider database of TUPs. Also, the application of the MimoSearch did not include any threshold adjustments to the search parameters, allowing for the tools to determine all potential target interactions in the BDB dataset. For the PSBinder, the prediction threshold was set at a default value of 0.5. This threshold denotes a moderate probability of binding with a higher threshold at 0.9 offering significant confidence level in the prediction process. With respect to the SGVYKVAYDWQH peptide, the PSBinder returned a probability of 0.91 which strongly demonstrated the peptide binding potential to polystyrene surfaces.

Overall, the application of these tools and settings in this study presents a comprehensive insight on the binding behavior attained thereby revealing its wide range of interactions, but equally unearthing a lack of specificity that aligns it more with TUP-like features instead of a specific mimotope.

## 3. Results and Discussions

### 3.1. SGVYKVAYDWQH: A specific mimotope?

The SGVYKVAYDWQH peptide has garnered substantial attention in recent BDB updates due to its high recurrence and frequent binding with various biological targets. Understanding whether SGVYKVAYDWQH functions as a specific mimotope is essential for harnessing its potential in therapeutics and research. Mimotopes are short peptides, typically 8 to 20 amino acids long [16], that mimic the structure of an epitope by binding to an antibody's antigen-combining site, despite being structurally distinct from the original antigen [5]. These mimotopes can be identified through phage display, mRNA display, ribosome display, and other combinatorial peptide library screening approaches. Several targets, ranging from metal ions, drugs to proteins, cells, and tissues, can be screened to identify mimotopes. The identification of mimotopes, especially through phage display experiments, is critical because of their potential applications in diagnostics, therapeutics, and vaccines. Their ability to elicit immune responses against specific pathogens or tumor cells makes them indispensable tools in disease treatment and immunotherapy [17, 18]. Additionally, mimotopes are valuable in elucidating protein-protein interaction networks [19–21] and may play pivotal roles in materials science and nanotechnology [22, 23]. In the case of SGVYKVAYDWQH, its classification as a mimotope hinges on determining whether it exhibits a specific binding affinity comparable to the natural



**Figure 1. Illustrations of the peptide SGVYKVAYDWQH binding behavior. The figure is created with the Generic Diagramming Platform (<https://BioGDP.com>) [24].**

target's binding site. According to BDB data, SGVYKVAYDWQH interacts with various targets, including non-biological molecules, cells, and proteins (as shown in Figure 1). Although this peptide shows broad binding spectrum, it may act as a mimotope if its binding characteristics mimic the template of the original target. The following sections review its interactions with various cellular, protein, and non-biological molecule targets, based on data curated from the BDB.

3.2. Cell and tissue targets

Table 1 highlights studies that identified SGVYKVAYDWQH as binders to cell or tissue models via phage display. Its notable use includes serving as a blood-brain barrier (BBB) shuttle peptide, selected through phage display on a human BBB cellular model. The peptide demonstrated moderate-to-high permeability across the BBB via clathrin-mediated endocytosis, indicating its potential for delivering therapeutic agents to the brain [25].

In another study, SGVYKVAYDWQH improved drug delivery to breast cancer (MCF7) cells, recognizing these cells with high affinity. The peptide was found in cell-binding phages, predominantly in the acidic eluate, which facilitated receptor-ligand interactions rather than non-specific hydrophobic interactions [26].

However, the peptide's journey was not always successful. For example, in a study targeting autoimmune myocarditis in mice,

SGVYKVAYDWQH initially showed potential by binding to homogenized mouse heart tissue during in vivo peptide screening. Yet, after the first round of screening, it was discarded due to insufficient results [27]. Similarly, it exhibited binding to Escherichia coli O157, but subsequent tests indicated low binding affinity, leading to its exclusion from further studies [28]. These results highlight both the promise and limitations of SGVYKVAYDWQH in cellular and tissue targeting applications. Practically, Figure 1 (A) illustrates the binding behavior of the SGVYKVAYDWQH peptide to distinct cell and tissue targets, with its role as a BBB shuttle peptide and its capacity to advance drug delivery to MCF7 breast cancer cells.

3.3. Protein targets

Table 2 presents data from 18 studies demonstrating SGVYKVAYDWQH's binding to various protein types, including antigens, antibodies, and receptors. For example, SGVYKVAYDWQH was selected for its affinity to CD133, a known cancer stem cell marker, and validated through ELISA [29]. The peptide also displayed affinity toward antibodies against Deinagkistrodon acutus venom and triosephosphate isomerase [30, 31]. Additionally, SGVYKVAYDWQH was isolated for binding to the monoclonal neutralizing antibody Y498 against human immunodeficient virus-1 [32], as well as to the envelope protein 2 of the chikungunya virus [33]. The peptide's binding affinities in all these studies were demonstrated by ELISA.

Despite these interactions, not all results were favorable. For instance, SGVYKVAYDWQH showed minimal binding affinity to the human epidermal growth factor receptor 2 (HER2), as undergoing a comparative biopanning experiment [34]. Similarly, it demonstrated weak binding to the insulin-like growth factor 2 receptor 1 and folate receptor alpha [35], leading to its rejection after affinity testing. The SGVYKVAYDWQH peptide construct (RNYK) mimics the brain-derived neurotrophic factor and has been reported to bind neurotrophic tyrosine kinase receptor type 2 (NTRK2). Its functional activity and binding affinity were confirmed using flow cytometry and MTT assays, demonstrating significant binding to the native NTRK2 structure in SH-SY5Y

**Table 1. Studies in which the SGVYKVAYDWQH was isolated with cells and tissue targets**

Target	Rd	Frequency	Affinity measurement	Reference
Human BBB	2	5/34	Fluorescence microscopy	[25]
MCF7 cell	4	6/68	Flow cytometry	[26]
Mice Heart	3	5/14	Fluorescence microscopy	[27]
E.coli O157:H7 cell	4	7/23	ELISA	[28]

**Table 2. Studies in which the SGVYKVAYDWQH was isolated with protein targets**

Target	Rd	Frequency	Affinity measurement	Reference
Cation-independent mannose-6-phosphate receptor (M6PR)	4,5	1/28, 16/28	ELISA	[1]
CD133 (ECD)	4	2/40	ELISA	[29]
Deinagkistrodon acutus venom (DA-pAb)	3	1/18	ELISA	[30]
Triosephosphate isomerase (TIM)	3	9	ELISA	[31]
Anti-HIV-1 monoclonal antibody Y498	3	13/42	ELISA	[32]
Envelope protein 2, E2	3		ELISA	[33]
human epidermal growth factor receptor 2 (HER2)	5	1/67, 37/57	ELISA	[34]
Folate receptor alpha (FR $\alpha$ )	4		ELISA	[35]
BDNF/NT-3 growth factors receptor NTRK2	4	11/15	ELISA	[36]
C-terminal half of human AHR	3		Fluorescence microscopy	[37]
extracellular domain of LDLR (ED-LDLR)	3		ELISA	[38]
E glycoprotein DIII	5	67/100	ELISA	[39]
Matrix metalloproteinase-9, MMP-9	4	8/19	ELISA	[40]
SECp43180	4			[41]
Amyloid beta 42, A $\beta$ 42	4	13	Fluorescence microscopy	[42]
Vitamin D binding protein, VDBP	4	1/9	ELISA	[43]
Bovine serum albumin (BSA)	4	7/10	ELISA	[43]
Vitamin D binding protein (VDBP) complex	4	7/15	ELISA	[43]

**Note:** Rd: round; ELISA: Enzyme-linked immunosorbent assay

cells in vitro [36]. Additionally, this peptide sequence was identified in a pool of peptides binding to the C-terminal half of the human aryl hydrocarbon receptor (AHR). When fused with GFP, the peptide successfully disrupted AHR function in cell cultures [37]. SGVYKVAYDWQH was also found to bind weakly to the low-density lipoprotein receptor, exhibiting a high dissociation constant indicative of low binding affinity [38]. Mertinková et al. employed Ph.D. 7-mer cyclic and 12-mer linear libraries for biopanning against Domain III (DIII) of the E protein, a critical receptor-binding domain for anti-flavivirus targeting. They observed frequent selection of the peptide and confirmed its interaction with rDIII using ELISA [39].

Furthermore, SGVYKVAYDWQH was selected as a binding candidate for other protein targets, such as matrix metalloproteinase-9, although its binding affinity was later dismissed through ELISA evaluation [39, 40]. In another study utilizing Ph.D.C7C and Ph.D.12 libraries, the peptide demonstrated binding to purified SECp43 180, a factor involved in selenocysteine biosynthesis and incorporation [41]. Figure 1(B) shows the SGVYKVAYDWQH binding behavior in protein targets.

Remarkably, SGVYKVAYDWQH also exhibited strong specificity and affinity for amyloid-beta 42 (A $\beta$ 42). After synthesizing the peptide, it was shown to bind to rA $\beta$ 42 with a tenfold higher affinity than previously described amyloid-binding peptides [42]. Lastly, in a pre-binding phage display approach, SGVYKVAYDWQH was found to bind vitamin D binding protein (VDBP), the VDBP complex, and even the negative control (BSA).

During the third biopanning, this sequence appeared four times on VDBP-coated plates, nine times on VDBP-Complex-coated plates, and four times on BSA-coated plates [43]. Despite being selected across numerous experiments, the peptide was frequently rejected due to low or insufficient affinities [32, 34, 36, 39, 40]. These mixed outcomes reflect the peptide's broad yet sometimes non-specific interaction profile with protein targets.

Figure 1(B) shows the binding behavior of the SGVYKVAYDWQH peptide to varied protein targets, demonstrating its diverse interactions with both non-specific and specific proteins. Thus, while the SGVYKVAYDWQH peptide exhibited strong affinities to certain targets such as amyloid-beta 42, its binding strength varied significantly across distinctive protein targets.

### 3.4. Non-biological molecule targets

Table 3 summarizes two studies focusing on SGVYKVAYDWQH's binding to non-biological molecules. Previous research has demonstrated that peptides can adhere to different organic and inorganic targets [44–48].

In one study, phage display screening was employed to identify adhesive domains specific to surfaces such as paper and laser printer toner. The SGVYKVAYDWQH peptide exhibited strong binding to printer toner but not to cellulose-based paper. Adsorption assays were conducted across different toner colors including black, yellow, magenta, and cyan blue to eliminate the potential

**Table 3. Studies in which the SGVYKVAYDWQH was isolated with non-biological targets**

Target	Rd	Frequency	Affinity measurement	Reference
Printed toner	4	3/16	Fluorescence microscopy	[49]
N-propyl paraben (PP)	3	5/15	Paraben Concentration Reduction Test	[50]
Polystyrene (PS)	3	1/15	Paraben Concentration Reduction Test	[50]
Methylparaben (MP)	3	2/13	Paraben Concentration Reduction Test	[50]

**Note:** Rd: round



influence of color pigments. Minor variations in binding were observed, indicating that the peptide's adsorption was primarily governed by interactions with the toner polymer [49].

In a separate study, the peptide was found to recognize methyl and N-propyl parabens, as well as polystyrene (used as a negative control). Adsorption assays revealed that SGVYKVAIDWQH had a stronger affinity for the paraben compounds than polystyrene [50]. These results indicate the peptide's selective binding potential, even for non-biological, chemically diverse molecules, reinforcing its versatility as a binding agent. Figure 1(C) shows the binding behavior of the peptide SGVYKVAIDWQH to varied non-biological molecule targets, revealing its strong affinity for substances like methyl, N-propyl paraben, and sprinter toner. These findings demonstrate the selective binding potential of the peptide to various chemical surfaces, further underscoring its versatility beyond biological applications.

### 3.5. SGVYKVAIDWQH: A TUP?

Despite its promising results, SGVYKVAIDWQH might also function as a TUP in many studies. TUPs are characterized by their ability to bind non-specifically to a wide array of molecular entities, regardless of target specificity [8]. The SGVYKVAIDWQH peptide has been found to interact with numerous proteins, small molecules, and even non-biological surfaces like printer toner [49, 50]. This broad binding profile, without a dominant interaction with a specific target, is indicative of TUP behavior. SGVYKVAIDWQH's ability to bind different cellular types and tissues further supports this hypothesis [25–27]. While it shows interactions with multiple proteins, its non-selective binding tendencies align it with the characteristics of established TUPs, such as SVSVMKPSRP, which also exhibits broad adhesive properties with minimal target specificity [13]. SGVYKVAIDWQH's versatility could make it a valuable tool in diverse therapeutic and research applications, but its lack of specificity raises concerns about off-target effects.

#### 3.5.1. Binding to polystyrene

Polystyrene is commonly used in assays like ELISA and as a substrate in cell cultures due to its biological inertness [51, 52]. While peptides that bind to polystyrene can be useful for immobilizing bioactive molecules, they are often regarded as TUPs due to their non-specific interactions [53, 54]. Several investigations have indicated that paraben toxicity poses risk to aquatic ecosystems and human health. Therefore, Lee et al utilized phage display technology for the identification of peptides that specifically bind to methylparaben (MP) and propylparaben (PP), which could facilitate the removal of paraben from wastewater [50]. Using MP-coated plate, PP-coated plate, and blank plate (polystyrene, negative control) as targets and following the paraben concentration reduction tests, they identified one MP-specific peptide DSQFNKYSIATV and one PP-specific peptide SWFSDWDELHA. However, SGVYKVAIDWQH not only appeared frequently in the results of the MP-coated plate but also PP-coated plate and blank plate, indicating it might be a peptide binding to polystyrene.

#### 3.5.2. PSBinder prediction results

The BDB integrates a suite of tools from SAROTUP [11], including PSBinder, a machine-learning-based tool designed to predict PSBPs from biopanning data or to identify new candidates for polystyrene affinity tags [14]. PSBinder uses a probability

threshold to distinguish between potential PSBPs, set by default at 0.5 but adjustable according to user needs. A probability threshold of 0.5 or higher predicts a peptide as a PSBP, though raising the threshold (e.g., to 0.95) can increase prediction confidence. For SGVYKVAIDWQH, PSBinder analysis returned a probability of 0.91, strongly suggesting that the peptide functions as a PSBP, or a selection-related TUP. This further underscores its potential role in non-specific binding to polystyrene surfaces and may guide future applications or refinements in experimental design.

#### 3.5.3. Meta-analysis according to BDB database and patents

Despite numerous publications and patents describing SGVYKVAIDWQH as a precise mimotope, recent evidence suggests a more complex reality. While early studies have emphasized the peptide's role in interacting with various biological targets, particularly in therapeutic and diagnostic contexts [34, 35, 41, 42], the analyses in this review indicate that SGVYKVAIDWQH may function more as a promiscuous peptide, possibly a TUP. Unlike specific mimotopes, characterized by their selective binding to a defined target, promiscuous peptides exhibit broad binding affinities, interacting with diverse biological materials and immunological receptors [55–57].

SGVYKVAIDWQH has demonstrated interactions with a wide range of tissues, proteins, and trivial molecules, reinforcing the notion that it may behave more like a TUP than a selective mimotope [27, 30–33]. Such peptides often bind non-specifically to multiple entities, indicating that SGVYKVAIDWQH may have been selected in experimental conditions for its non-specific, broad binding properties rather than for precise target recognition [1, 27, 30–38]. This is further supported by its interactions with both biological and non-biological targets, as highlighted in this comprehensive analysis of binding data, including the results from PSBinder, which suggests the peptide's promiscuous binding nature rather than specificity [27, 30–38, 49, 50]. This distinction between SGVYKVAIDWQH's perceived specificity in the literature and its demonstrated promiscuous binding has important implications. On the one hand, promiscuous peptides can offer the potential for applications such as cross-protection vaccines or epitope mapping in varied research contexts [58, 59]. On the other hand, their non-specific binding can lead to off-target effects and unintended outcomes, complicating their practical use in precision applications [60, 61].

Our review of both patents and literature supports the conclusion that SGVYKVAIDWQH interacts with several biological and non-biological targets, reflecting characteristics of a TUP or promiscuous peptide. This broad binding profile raises concerns about its functionality as a specific mimotope, suggesting that its selection may be driven more by non-specific affinity to the screening systems [7–9].

Significantly, given the unique and broad nature of the SGVYKVAIDWQH, its non-specific binding profile perfectly aligns it with the cluster of selection-related TUPs. These kinds of peptides tend to interact with contaminants of present in the screen system, instead of biological target. In this study, it was observed that SGVYKVAIDWQH frequently binds to several surfaces which include non-biological ones like polystyrene as well as to broad range of tissues and proteins. The results based on PSBinder analysis further validate this, as they suggest SGVYKVAIDWQH exhibits high probability of being a polystyrene-binding peptide (PSBP) thereby demonstrating its interaction with constituents of the screening system. Whereas propagation-related TUPs which are considered as selected based on their rapid replication within host cells, SGVYKVAIDWQH's

selection seems to be driven by its promiscuous binding properties, instead of any advantageous replication rate or behavior within the host. The Phd7Faster 2.0 tool was applied to predict if SGVYKVAYSWQH is a propagation-related TUP. The result returned NO with a probability of 0.34 [62]. The tool Phd7Faster 2.0 is developed for screening the panning result of the Ph.D.-7 phage display library and SGVYKVAYSWQH is from the Ph.D.-12 phage display library. However the two types of libraries are constructed with the same vector and produced by the same company. Thus, it is somehow reasonable to be used for the Ph.D.-12 phage display library. Therefore, the SGVYKVAYDWQH is been categorized as section-based TUPs that demonstrates its potential non-specific interactions in varied screening systems instead of a role in host cell propagation.

#### 4. Conclusion

The study of SGVYKVAYDWQH reveals a dual potential as both a promiscuous peptide and a TUP. While some studies suggest it is a specific mimotope, its broad, non-specific binding behavior aligns it with the traits of TUPs. Its ability to mimic specific protein binding features in certain contexts such as interactions with some antibodies, antigens, and receptors raises the possibility that SGVYKVAYDWQH may serve as a functional mimotope. However, its frequent interactions with such many different targets imply that it may often function as a TUP, with non-specific binding across various entities. Some further analysis, particularly with respect to its interactions with different cell types and organ tissues, demonstrates the peptide's potential in diagnostic imaging and drug delivery. However, some studies have excluded SGVYKVAYDWQH due to its weak binding in certain instances. This variability in binding necessitates further validation or optimization for specific uses.

The peptide's interactions with proteins involved in autoimmune diseases, cancer, and viral infections also imply its potential role in therapeutic research. However, further investigation is required to determine whether its primary utility lies in a specific targeting or just serving as a more general non-specific binding agent.

The application of Phd7Faster 2.0 tool was deployed to predict if SGVYKVAYSWQH is a propagation-related TUP [62]. Although the peptide SGVYKVAYDWQH does not exhibit TUP motifs or behavior in earlier analysis (as earlier TUPScan analysis in BDB database and TUPDB suggests), PSBinder analysis returned a probability of 0.91, strongly suggesting that the peptide functions as a PSBP, or a selection-related TUP.

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#### Ethical Statement

This study does not contain any studies with human or animal subjects performed by any of the authors.

#### Conflicts of Interest

Jian Huang is the Associate Editor for Medinformatics and was not involved in the editorial review or the decision to publish this article. The authors declare that they have no conflicts of interest to this work.

#### Data Availability Statement

The data that support the findings of this study are openly available in Biopanning Data Bank at <https://i.uestc.edu.cn/bdb/>, reference number [12], and Google Patents at [https://patents.google.com/?q=\(SGVYKVAYDWQH\)&oq=SGVYKVAYDWQH](https://patents.google.com/?q=(SGVYKVAYDWQH)&oq=SGVYKVAYDWQH).

#### Author Contribution Statement

**Hamza B. Abagna:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Data curation, Writing – original draft, Writing – review & editing. **Samarappuli Mudiyansele Savini Gunarathne:** Formal analysis, Investigation, Data curation. **Yuqing Jiang:** Formal analysis, Investigation, Data curation. **Jian Huang:** Conceptualization, Methodology, Validation, Resources, Writing – review & editing, Supervision, Project administration, Funding acquisition.

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