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Investigating Oncological Properties of Transactivation Domain of the p53 using Computerized Digital Signal Processing-based Bioinformatics Technique: A Demonstration

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Abstract

Background: We preliminarily advocated for multidisciplinary-based American centers for calculation the of biological bio-functionalities where robust computerized techniques will be used to investigate varieties of illnesses including Cancer; and further design and develop therapeutic interventions. Genetic variations in p53 have been associated with Cancer as well as conferment of novel features. Understanding these variations will help proffer therapeutic interventions.

Aim: To help validate the reliability of these procedures, mutation-induced (L22Q, W23S, W53Q, and F54S) abrogation of transcriptional activity, clinically observed from the Transactivation Domain (TAD1 and TAD2) of the p53 was computationally re-assessed. Steps involved in investigating this oncological characteristic using this computerized bioinformatics-based procedure are demonstrated as a guide.

Method: A Digital Signal Processing procedure called Informational Spectrum Method (ISM) is employed on the protein sequences of p53 and its motif, TAD using 7 Amino Acid Scales (AASs). ISM entails translation of the protein sequences into numerical sequences (signals) using appropriate AASs and subsequent analysis by means of Discrete Fourier Transform.

Results: Our findings revealed that different AASs provided different consensus frequencies or positions of common interactions. Similarly, the oncogene, p53 and its fragment TAD both provided different positions of common interaction. Additionally, concomitant engagement of all mutants provided 100% activity. Other ASSs are envisaged to provide complimentary results.

Discussions: These findings appear to suggest that the steps needed in oncological examinations requires engagement of the proteins involved (and not their fragments or whole genome). The results favored concomitant use of all mutants. This proce-dure has earlier proffered investigations into over 1000 pro-teins, designed pro-active drugs and vaccines, online bioinfor-matics tools (such as ISTREE) and biomedical devices including Computer-Aided Drug Resistance Calculator (US20150370964).

Conclusion: This computerized approach rationalizes, may revolutionize oncological investigations and provide a guide for all biological investigations. Because it depends on protein se-quence information, it will further help design and assess the activities and suitability of monoclonal antibodies, a major source of emerging therapy for cancer, COPD, and others, inluding reports that single point mutation (S49R) in the EC domain of the EGFR abrogates binding inter-action with a monoclonal antibody therapy (Cetuximab) unlike another called Panitumumab, rendering Cetuximab less effective. Es-tablishment Onco-informatics specialty has become paramount.

Keywords: Bioinformatics; Digital signal processing; Informa-tional spectrum method; p53; Transactivation domain

Introduction

Good understanding of disease processes is needed to proffer therapeutic solutions. Earlier solutions including Anti-Microbial Resistance (AMR), which engage assay techniques such as Culture and Sensitivity tests have been provided. These techniques utilize slow and resources-consuming clinical techniques [1-3]. However, computerized procedures including Discrete Fourier Transform (DFT)-based, Digital Signal Processing (DSP) techniques are known to be faster, resource-saving [4], and have taken over assessments in several fields. They are now being incorporated into several specialties resulting in new fields like Immuno-informatics [5], Nano-informatics [6], Geo-informatics [7] and others.

According to a study [8], over 50 genes have been implicated in the p53-regulated bio-functionalities including cell cycling, cell death (apoptosis), cell differentiation, cellular senescence (cessation of cell replication), angiogenesis (growth of new blood vessels) and elimination of the damaged DNA, resulting in over 20,000 tumors [8]. Mutations associated with transcription are investigated in this study.

Transcription refers to the process of replicating genetic information kept in the DNA strand into messenger (matching) RNA by means of RNA polymerase enzyme [10]. Wild-type p53 is known as an effective transcriptional activator. However, p53 mutants have been recognized to trans-activate multitudes of genes [9], providing opportunities for diverse interactions with other genes. Studies have shown that wild-type p53 concentrates its transcriptional activities on the promotion of cell cycle arrest or programmed cell death [9] while the activities of the p53 mutants transcend into other biological activities, which have targets (protein or genes) or genes expressing the interactions.

Most of the oncogenic mutations have been recognized to be entrenched in the DNA-binding domain (DBD). However, few have been isolated from other motifs including the Transactivation domain (TAD) [8–10]. These motifs regulate transcriptional activities. The motifs compose of the 1-61 amino acid lengths of the p53 [8,9]. p53 (wild-type) depends on the four essential hydrophobic components (L22, W23, W53 and F54) of the TAD1 and TAD2 to exert its transactivation characteristic [8,9]. These hydrophobic protein residues with polar amino acids and bring about abrogation of transactivation property, by means of the four mutations (L22Q, W23S, W53Q, and F54S) [8,9].

Out of the 565 available Amino Acid Scales [11], seven are engaged. They are Kyte-Doolittle, Electron Ion Interaction Potential (EIIP), CHAM830107, CHAM830108, KLEP840101, FAUJ880111, FAUJ880112 [12]. EIIP accounts for binding interaction [12–14,] while Kyte-Doolittle represents Hydrophobicity interaction [12]. CHAM830107, CHAM830108, KLEP840101, FAUJ880111, FAUJ880112 express Charge Transfer in the form of Positive, Negative and Net Charges, respectively [12,15]. These AASs are chosen because they govern physio-chemical properties involved (Hydrophobicity and Polar Charges) [8,9]. To unveil the totality of this biological feature, all the parameters involved in the interactions must be engaged, and the results are aggregated [11]. This is because it has been reported that at one-point mutation, several AASs are involved [11]. AAS refers to the degree of participation by each of the 20 essential amino acids in an interaction.

By translating protein residues into signals and subsequently decomposing them using DSP technique (Discrete Fourier Transform (DFT)), some researchers ushered in a novel procedure to uncovering biological characteristics hidden in proteins [13]. This invention presented two physio-mathematical techniques called Resonant Recognition Method (RRM) [14–17] and Informational Spectrum Method (ISM) [13,18-40].

Decomposition of numerical sequences (signals) using DFT brings about numerous peaks, each representing a biological characteristic. Both techniques had fetched investigations into more than 1000 proteins including oncogenes [14] such as interactions that exist between the pro-oncogene refer to p53 and (its mediator) MDM2 [23]; antitumor regulatory activities of TNF, IL-2, IFN-beta, and human M-CSF were investigated using RRM [15]. ISM has provided a common position of interaction for p53 and its mediators [23].

As a guide to ISM-based computerized approach to assessing oncological assessment, this preliminarily and clinical verified abrogation of transcriptional activity found in the Transactivation Domains (TAD1 and TAD2) of the p53 resulting from four mutations (L22Q, W23S, W53Q, and F54S) [9] is therefore computationally re-examined.

Similar study has been carried out using Plasmodial protein. Abrogation of pharmacological inactivity resulting from a single mutation in the Duffy Antigen Receptor Chemokines (nDARC Y41F) protein found in the Plasmodial peptide (nDARC) peptide has computationally been verified [25]. Preliminarily, this study has clinically been ascertained [42]. Computational re-examination using the five affected AASs revealed that the decreased activity (84.4%) demonstrated by the wild type nDARC was restored to 100% activity due to the introduction of a single mutation nDARC Y41F [25].

As huge sequence information is daily obtained especially in the field of cancer, transforming them into oncological properties using bioinformatics approaches (Translational Bioinformatics) has become vital in the assessment, designing and development of both anti-cancer therapy and personalized medicine [43]. Employing these procedures especially in monoclonal antibodies is needful as they have become a major source of therapies in diseases like Cancer, Diabetes, Rheumatoid diseases, COPD. Reports have shown that though single point mutation (S49R) in the EC domain of the EGFR abrogates binding interaction with a Monoclonal Antibody therapy (Cetuximab), this mutation does not have effect on another Monoclonal Antibody therapy (Panitumumab) [44–46]. This may explain why Cetuximab is less effective [46]. Establishment of a new field that will concentrate on information technology-oriented studies using these computerized procedures on cancer studies (Onco-informatics) has also become necessary.

The results are presented in the next section.

Method

Material

The materials consist of 393 and 61 amino acid lengths of the p53 and its Transactivation Domain (TAD), respectively (Figure 1) [9,10], as well as seven Amino Acid Scales (AASs). The Consensus sequences are obtained from UNIPROT database [47]. The AASs are Kyte-Doolittle, EIIP, CHAM830107, CHAM830108, KLEP840101, FAUJ880111, FAUJ880112 [12]. Table 1 is the corresponding EIIP numerical values for the 20 essential amino acids.

Figure 1: Showing (A) the 393 amino acid-length (complete) protein residues of p53 and (B), the 61-amino acid length p53 Transactivation Domains 1 and 2 (TAD 1 and 2) indicating the positions of mutations (L22Q, W23S, W53Q and F54S).

Amino Acid	AAS value	Amino acid	AAS value	Amino Acid	AAS value	Amino acid	AAS value
A	0.0373	Q	0.0761	L	0.0242	S	0.0829
R	0.0959	E	0.0058	K	0.0371	T	0.0941
N	0.1263	G	0.0050	M	0.0823	W	0.0548
D	0.0036	H	0.0242	F	0.0946	Y	0.0516
C	0.0829	I	0.0242	P	0.0198	V	0.0057

Table 1: Electron Ion Interaction Potential (EIIP), showing numerical values representing the level of binding interaction as provided by each of the 20 essential amino acids.

The Procedure

Informational Spectrum Method (ISM) is employed here. The procedure is briefly described here. It has already been detailed in [13,18–23,25,29,33,34]. ISM consists of three major steps.

Conversion of the Protein Primary structure (Amino Acid Sequences) into Numerical Sequences (Signals) using seven Amino Acid Parameters:

This is the initial step in the ISM process. Each Amino Acid Scales (AASs) engaged in the interactions has numerical values representing the contribution offered by each of the 20 essential amino acids. Each amino acid sequence therefore is converted into numerical sequences using the corresponding contributions provided by each of the 20 essential amino acids. The numerical sequences are called signals. As signals, they are qualified for decomposition and analysis using any Digital Signal Processing technique such as Discrete Fourier Transform used here. In a situation where the sequences are unequal in length, zero values are added to bring the sequences to equal length. This is called Zero-padding.

Discrete Fourier Transform-based Processing of the Signals (Informational Spectrum):

This step entails decomposing these series of signals using Discrete Fourier Transform (DFT). The DFT decomposition is expressed as:

$$X(n) = \sum_{k=0}^{N-1} x(k) e^{-j2\pi kn/N} \qquad \text{Equation 1}$$

Where

n is the discrete time index that runs from 0 to N-1. k is the discrete frequency index that traverses 0-N/2 as one part of the mirror (symmetric) image is used. X(k) expresses the m member of the numerical series. N is the length of the numerical sequence. X(n) represents the coefficient of the DFT.

DFT decompositions usually give rise to both real and imaginary component. This is because they are sum of both sine and cosine waves. Absolute components are derived as:

$$X(n) = [R(n) + I(N)j] \qquad \text{Equation 2}$$

Where n = 1, 2, ..., N/2, R and I express the Real and Imaginary parts each.

The Absolute Spectrum representing the magnitude of interaction as amplitudes is expressed as:

$$S_a(n) = X(n)X^*(n), \text{ which is equal to } |X(n)^2| \qquad \text{Equation 3}$$

Where Sa represents the Absolute Spectrum, X(n) the DFT coefficient, and X(n) indicates the conjugate component, while n ranges from 0-N/2.*

Plots of the magnitude of interaction (amplitudes) on the y-axis and frequencies on the x-axis are referred to as Informational Spectra (IS). Each peak represents degree of interaction with other bio-molecules with regards to the bio-functionality investigated as typified by the AAS engaged.

Point-wise Multiplication of the Signals (Common Informational Spectrum):

The position of common interaction is determined by point-wise multiplication of the Informational Spectra (IS), which are derived by processing the numerical sequences (signals) using Discrete Fourier Transform. Point-wise (element-wise) multiplication is a mathematical operation (multiplication) that occurs with regards to individual points in the space (in this case, sequences) [24]. It is expressed as:

$$C_a = \prod S(a)(m) \qquad \text{Equation 4}$$

Where:

Ca is the Common Informational Spectrum characteristics. $\prod$ *is the point-wise multiplication function.*

S(a) is still the Absolute Spectrum. m = 1, 2, 3, ...M and M represents the number of protein sequences involved

According to the principles of ISM [13] and RRM [14], biomolecules with common biological characteristics demonstrate a maximum peak at the common point of interaction. This position is called Consensus Frequency (CF), which is calculated as:

$$CF = PP/N$$

Where:

PP is the Peak Position and N is the length of the longest protein investigated.

The degree of contribution by each sequence at the CF with respect to the biological characteristic are then calculated (numerically obtained) as the magnitude of interaction. To obtain total bio-functionality, and in this case oncological properties, all mutants and wild types as well as the AASs must be engaged as several AASs have been implicated in a single sequence change (11).

Results

Informational Spectrum Method-based analysis of both p53, which is compose of 393 protein residues and its 61 membered fragment, TAD, using seven Amino Acid Scales resulted in hundreds of peaks (Tables 2 and 3, and Figures 2–7). Each peak represents an interaction or intra-action with other bio-molecules, a bio-functionality, which could be a physio-chemical or structural as depicted by the AAS in use. Peaks including those at the point of common interaction are examined.

The results are presented in tables 2 and 3, and figures 2–7. Oncogene p53 is processed using the seven AASs. EIIP and Kyte-Doolittle only are applied on TAD.

Consensus Frequency (CF)/Position of Common Interaction:

EIIP and Kyte-Doolittle:

As shown in Tables 2 and 3, the Consensus Frequencies (CFs) or common positions of interaction for TAD and p53 using EIIP are 0.278 and 0.031, respectively. Similarly, by means of Kyte-Doolittle, TAD and p53 presented CFs at 0.230 and 0.252, respectively.

Other AASs:

Table 2 and 3 indicate that while CHAM830107 and CHAM830108 displayed CFs at 0.473 and 0.252 each, KLEP840101, FAUJ880111 and FAUJ880112 demonstrated CFs at 0.313, 0.204 and 0.018, respectively.

	Protein	Amino Acid Parameter	CF
1	TAD	EIIP	0.278 (17)
2	p53	EIIP	0.031 (12)
3	TAD	Kyte-Doolittle	0.230 (14)
4	p53	Kyte-Doolittle	0.252 (99)
5	P53	CHAM830107	0.473 (186)
6	P53	CHAM830108	0.252 (99)
7	p53	KLEP840101	0.313 (123)
8	p53	FAUJ880111	0.204 (80)
9	p53	FAUJ880112	0.018 (7)

Table 2: Consensus Frequency (CF)/Position of Common Interaction using Kyte-Doolittle and EIIP.

Percentage biological activities as expressed by wild types and mutants

Table 3 is the percentage biological activities in terms physio-chemical properties (binding interaction, hydrophobicity and charge transfer) using seven AASs, and as expressed by the p53 and its motif, TAD, at positions including the points of common interactions. Except position 78 of the EIIP-based results of the analysis of p53, others are the positions of common interactions (Table 3, column 4). The result shows that only an individual mutant, W23S demonstrated 100% activity. All mutants yielded 95.5%.

All AASs but CHAM830107, KLEP840101, FAUJ880111 and FAUJ880112 demonstrated differences in the level of interactions at the positions of common interaction. Both the wild-type and the mutants showed same level of interaction (100%). Except the Kyte-Doolittle, all other AASs demonstrated highest interaction (100%) at the CFs when the four mutations are engaged simultaneously.

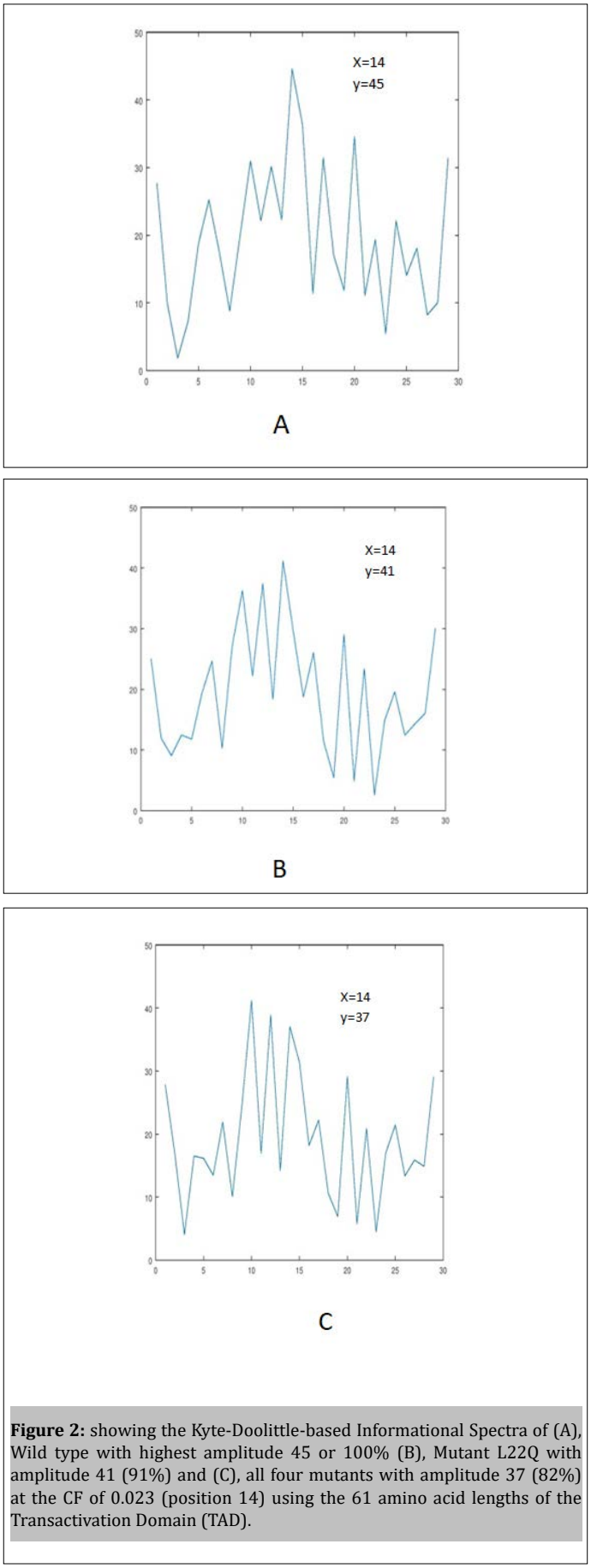
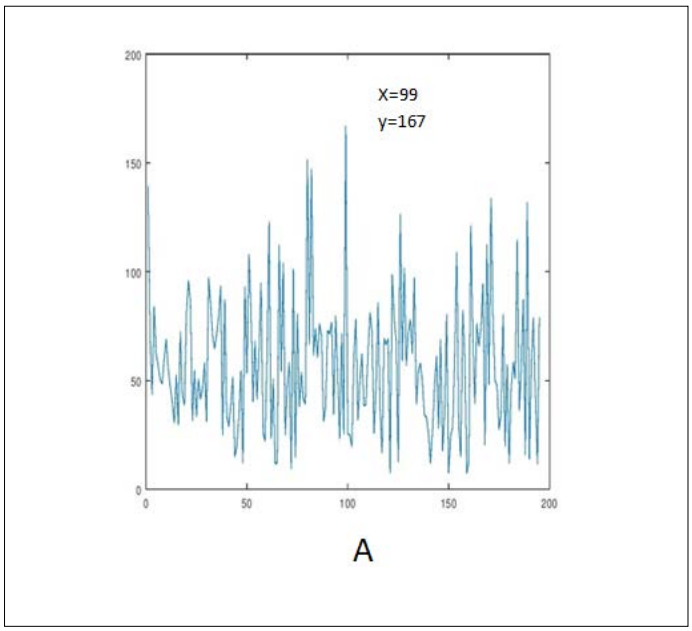
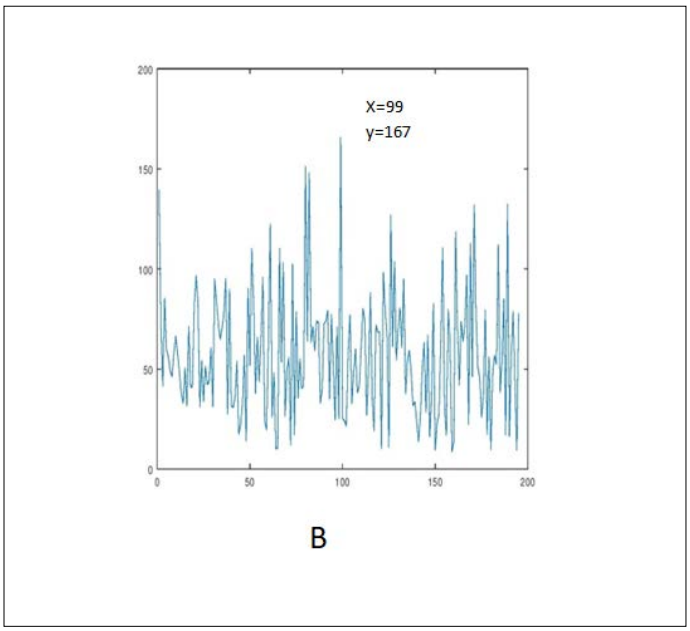


Figure 2: showing the Kyte-Doolittle-based Informational Spectra of (A), Wild type with highest amplitude 45 or 100% (B), Mutant L22Q with amplitude 41 (91%) and (C), all four mutants with amplitude 37 (82%) at the CF of 0.023 (position 14) using the 61 amino acid lengths of the Transactivation Domain (TAD).

	1	2	3	4	6	7	8	9	10	11
1	Mutant	EIIP (TAD)	EIIP (P53)	EIIP (p53) at 78	Kyte-Doolittle (p53)	CHAM830107	CHAM830108	KLEP840101	FAUJ880111	FAUJ880112
2	CF	0.278 (17)	0.031 (12)	Not Applicable	0.252 (99)	0.473 (186)	0.252 (99)	0.313 (123)	0.204 (80)	0.018 (7)
3	wild type	0.66 (94.3%)	2.60 (95.2%)	2.60 (99.2%)	167 (100%)	21.00 (100%)	25.6 (96.5%)	28.8 (100%)	16.00 (100%)	16.7 (100%)
4	L22Q	0.70 (100%)	2.70 (98.9%)	2.54 (97%)	161 (96.4%)	21.00 (100%)	26.5 (100%)	28.8 (100%)	16.00 (100%)	16.7 (100%)
5	W23S	0.69 (98.6%)	2.65 (97.1%)	2.62 (100%)	167 (100%)	21.00 (100%)	24.8 (93.6%)	28.8 (100%)	16.00 (100%)	16.7 (100%)
6	W53Q	0.65 (92.9%)	2.63 (96.3%)	2.61 (99.6%)	167 (100%)	21.00 (100%)	25.6 (96.6%)	28.8 (100%)	16.00 (100%)	16.7 (100%)
7	F54S	0.66 (94.3%)	2.62 (96%)	2.61 (99.6%)	167 (100%)	21.00 (100%)	25.4 (95.9%)	28.8 (100%)	16.00 (100%)	16.7 (100%)
8	All	0.70 (100%)	2.73 (100%)	2.50 (95.4%)	162 (97.0%)	21.00 (100%)	25.3 (98.8%)	28.8 (100%)	28.8 (100%)	16.7 (100%)

Table 3: Percentage biological activities as expressed by wild types and mutants using seven Amino Acid Parameters.





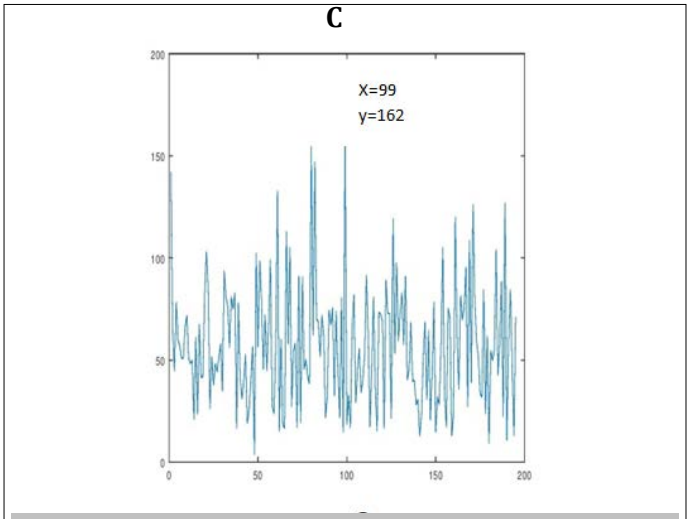


Figure 3: showing the Kyte-Doolittle-based Informational Spectra of (A), Wild type with highest amplitude 167 or 100% (B), Mutant W23S with amplitude 167 (100%) and (C), all four mutants with amplitude 162 (97.0%) at the CF of 0.252 (position 99) using the 393 amino acid lengths.

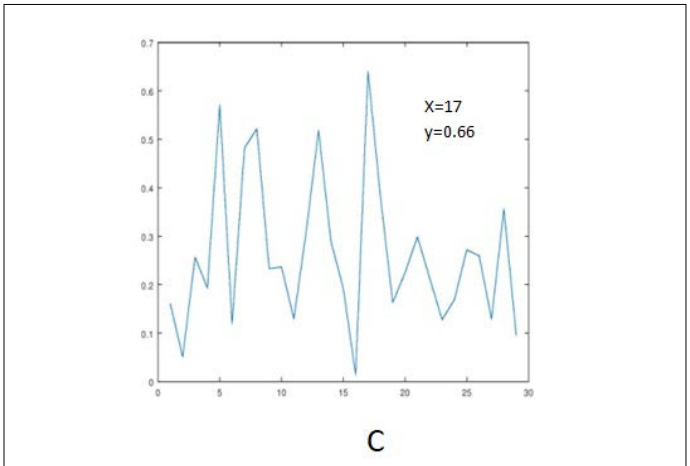
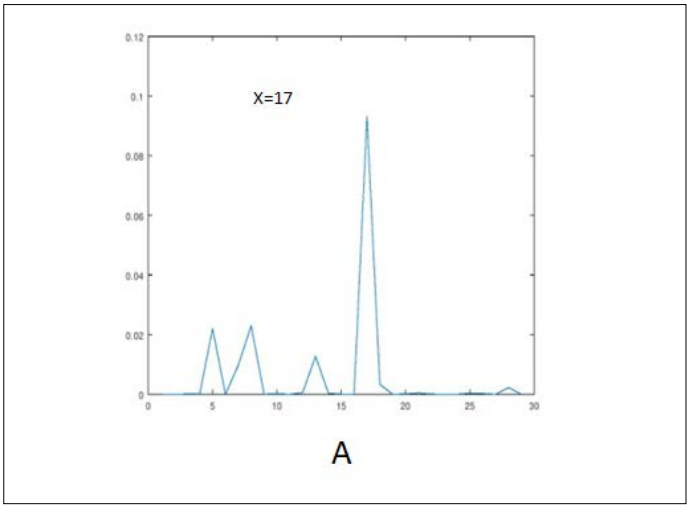
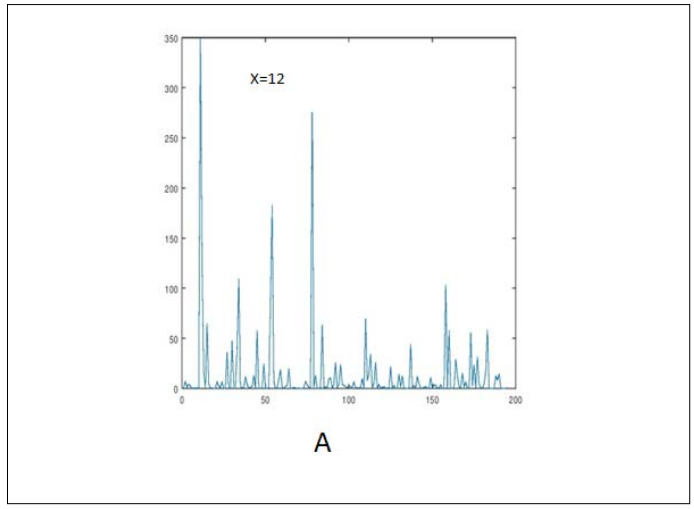
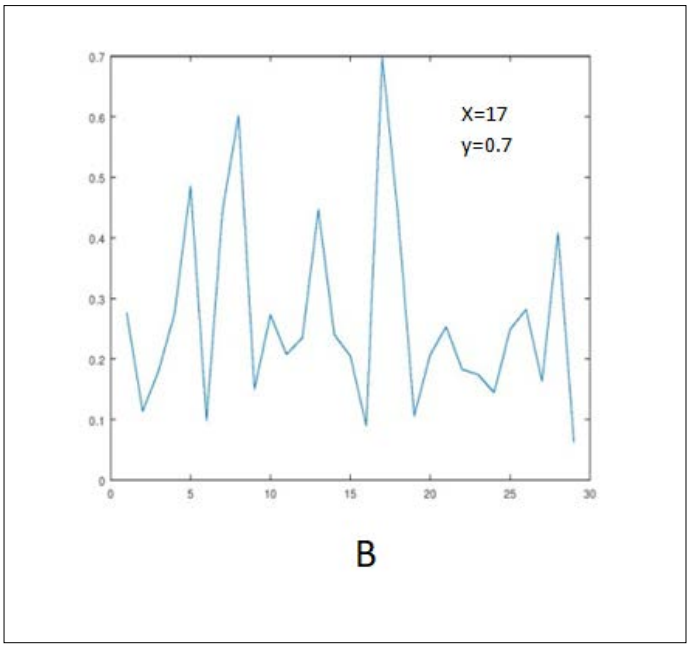
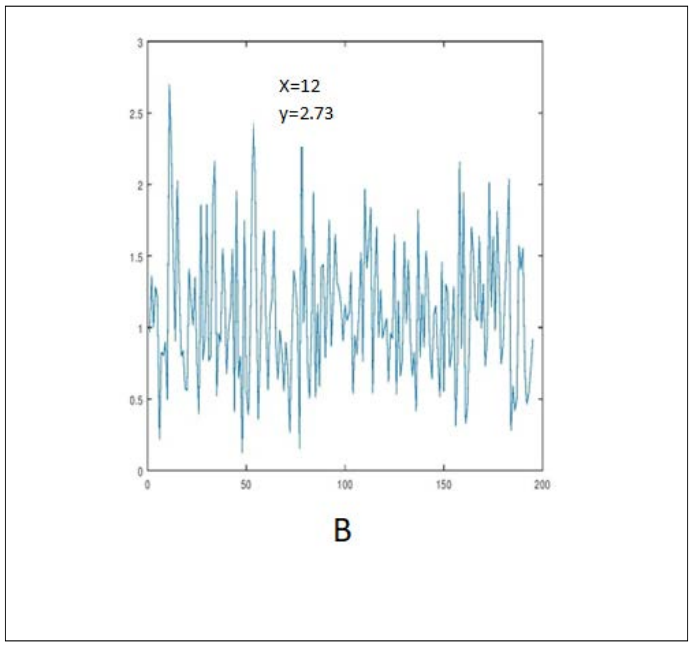


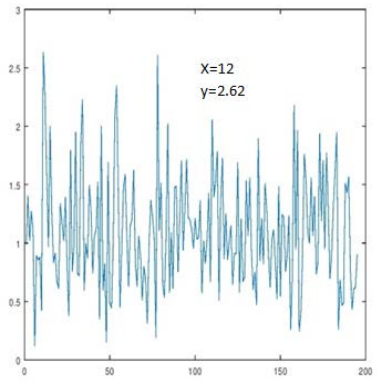
Figure 4: *showing the EIIP-based (A) Common Informational Spectrum of all sequence indicating CF at f=0.278 (position 17); Informational Spectra (B), Mutants L22Q and (C), F54S displaying highest amplitude of 0.70 (100%) and 0.66 (94.3%), respectively using the 61 amino acid lengths of the Transactivation Domain (TAD).*





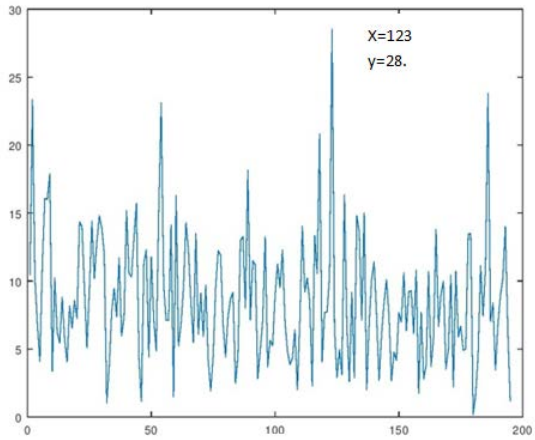




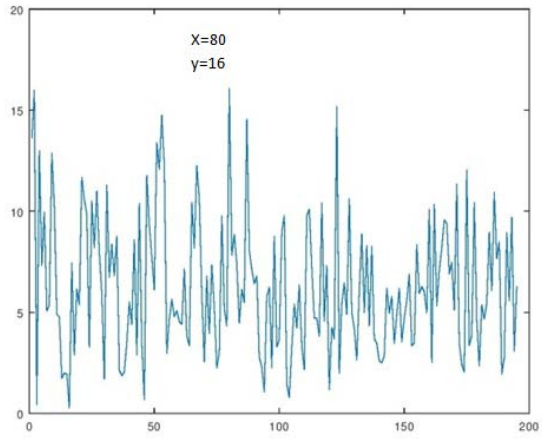


C

Figure 5: EIIP-based (A) Common Informational Spectrum indicating CF at 0.031 (position 12), Informational Spectra (B) all mutants, (C) F54S, with amplitude 2.73 (100%) and 2.62 (96%), respectively using 393 amino acid lengths p53

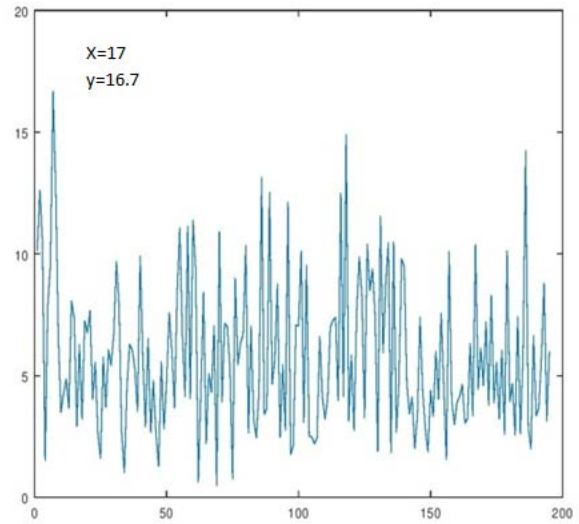


A

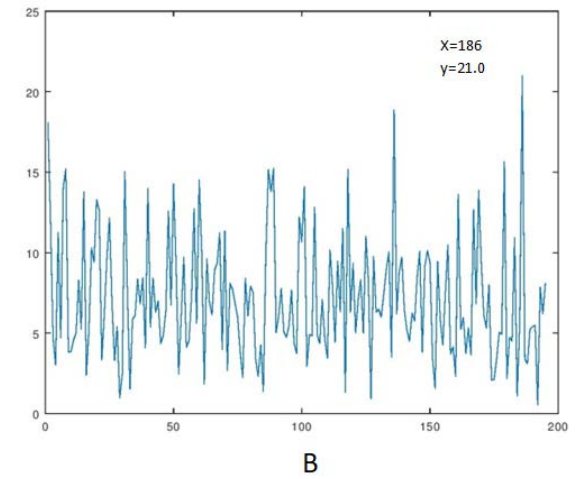


B

Figure 6: Informational Spectrum of the wild type (consensus sequence) of the p53 using (A) KLEP840101 and (B) FAUJ880111 indicating 100% interaction by each sequence at CFs of 0.313 (position 123) and 0.204 (position 80).



A



B

Figure 7: Informational Spectra of the wild type (consensus sequence) only, of the p53 using (A) FAUJ88012 (B) CHAM830107 indicating 100% interaction each at their respective CFs 0.018 (position7) and f=0.473 (position 186).

Discussions

In this section, the interpretation of the peaks generated using the ISM procedure and seven AASs on 61 and 393 amino acid lengths of the TAD and p53, respectively are presented. Each peak represents a biological functionality based on the proteins that share the CF and the AAS engaged.

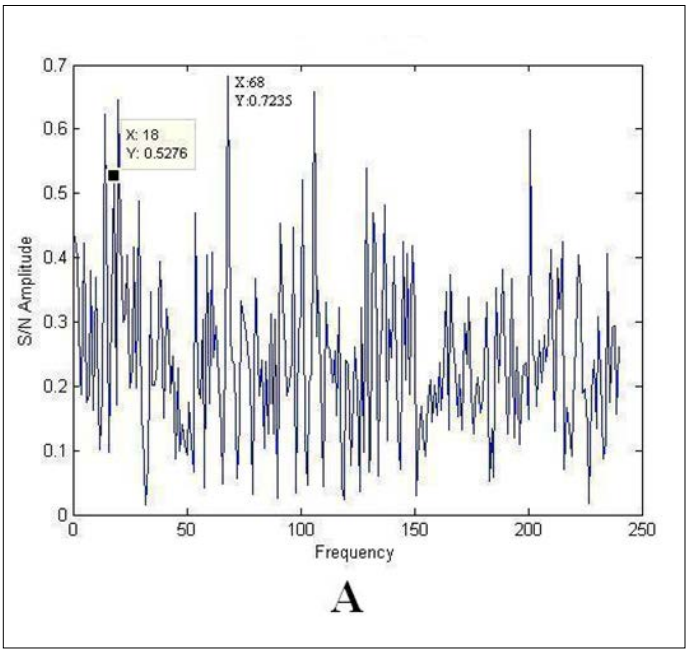
There are eight highlights that guided how this computerized procedure would be employed on oncological evaluations:

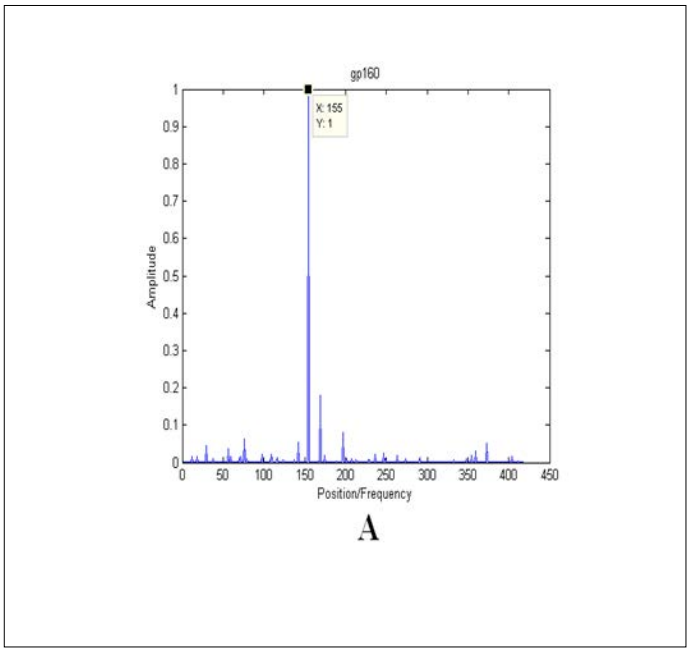
1. At peak (frequency = 0.0373 or position 18), CD4s of the HIV hosts including Human and Chimpanzee, as preliminarily studied, demonstrated point of common interaction with the HIV gp120 obtained from several isolates [17,25,34,38]. Based on this, several biological characteristics were examined including the mechanism by which HIV infection translates to AIDS [25,38] and the prediction of HIV tropism [25,34]. Similarly, this signifies that common positions of interaction with other proteins will help unearth other biological characteristics of the oncogenes.

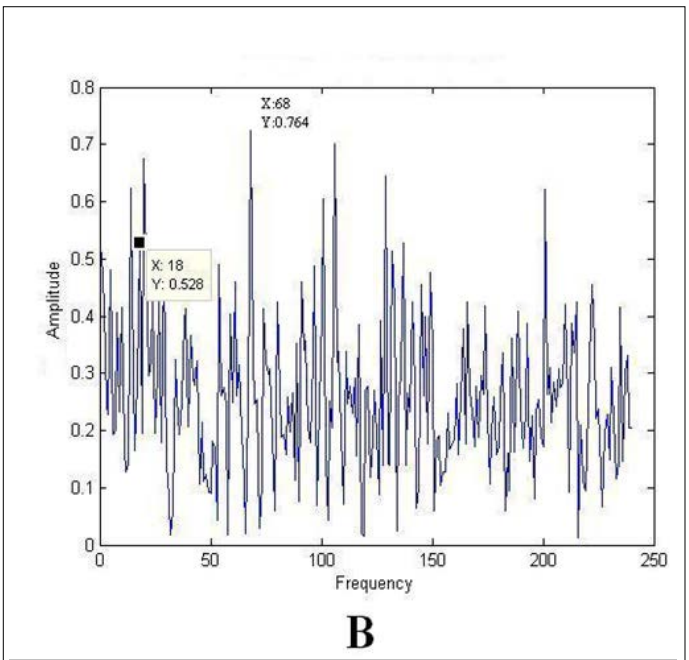
2. As shown in figure 8, at another peak (frequency = 0.14 or position 68) both CD4s of Human and Chimpanzee demonstrated maximum binding interaction [37]. Both species have earlier been found to originate from same source. This biological characteristic is observed in other HIV strains including 98US_MSC5016 and 98US_MSC5007 isolated from American soldiers on Foreign Service. This property helped identify that they may have originated from Zaire and Nigeria, respectively [37]. This is because, the gp120 of 98US_MSC5007 and a Nigerian isolate (92NG083) were found share same position of maximum interaction [37]. Similarly, 98US_MSC5016 and the Zairian isolates (ELI, MAL, and Z2/CDC-34) have very close position of maximum interaction.

For engagement in the oncological investigations, it is therefore proposed that every peak will be considered for a bio-functionality.

3. It was revealed in this study that EIIP- and Kyte-Doolittle-based analysis of p53 and its motif, TAD demonstrated different positions of common interaction or CFs (Table 2 and Figures 2 and 3). For example, EIIP revealed a position of common interaction (CF) at 0.278 and 0.031 for TAD and p53, respectively. In the case of Kyte-Doolittle, TAD and p53 presented CFs of 0.230 and 0.252, respectively. It must be noted that TAD is only a domain of the oncogene, p53. It is therefore important to note that the clinical investigation of oncological property is directed to the oncogene, p53 and not its fragment.







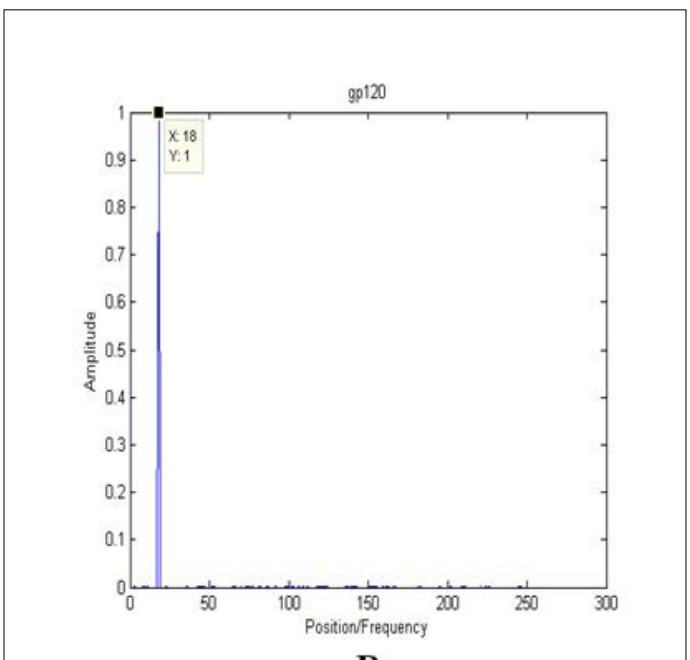


Figure 8: EIIP-based Informational Spectra of the protein residues of the CD4 belonging to (A) Human and Chimpanzee, showing 52.78% and 52.8% levels of binding interaction at positions 18 (CF = 0.0373); as well as 72.35% and 76.4% at position 68 (f = 0.14) (courtesy of [25,38]).

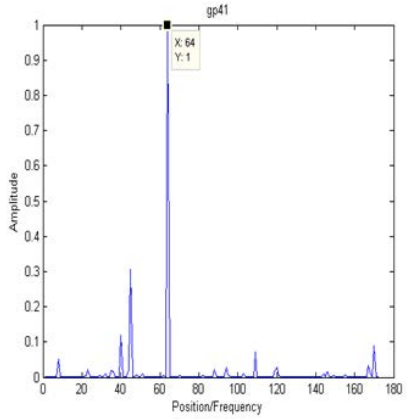


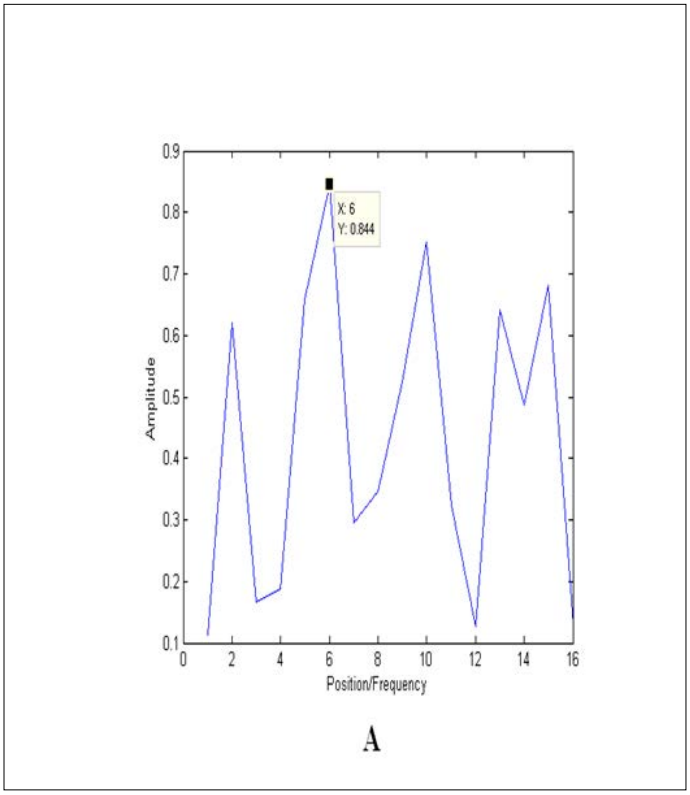
Figure 9: Common Informational Spectra of the HIV (A) Envelope or gp160 (B) Surface or gp120, and (C) Transmembrane Proteins or gp41 showing CFs at 0.185, 0.0354 and 0.186, respectively (courtesy of [25,38]).

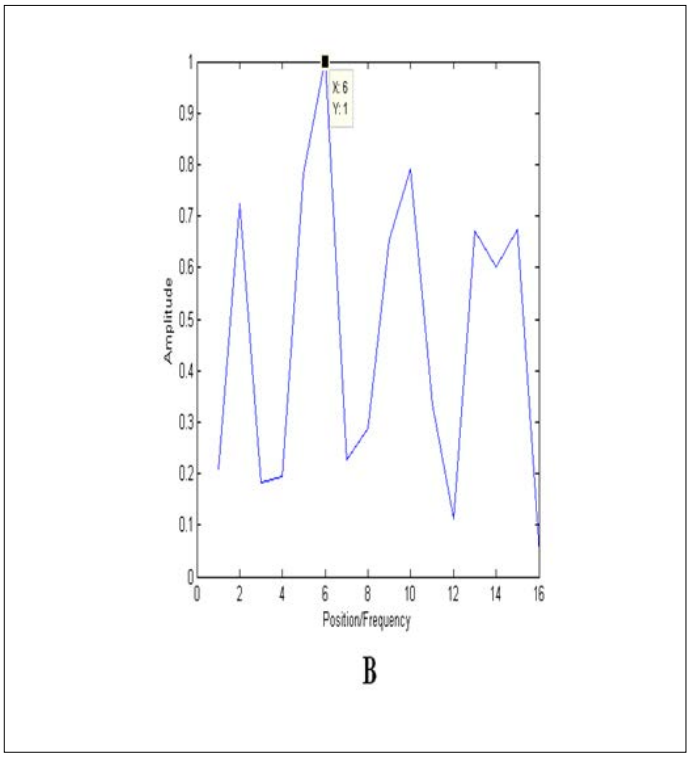
4. We have earlier shown that the CFs of HIV Envelope protein (gp160) and its two components Surface (gp120) and Transmembrane proteins (gp41) share different positions of common interaction (Figure 9). The only CF that corresponded to the CD4 belongs to the Surface protein. Clinically, interaction between the HIV gp120 and CD4 has been verified [45]. Computationally, this has also been validated using RRM [17] and ISM [25]. Since the ISM-based analysis of the oncogene, p53 and its segment TAD demonstrated different CFs, it is recommended that ISM-based oncological studies be channeled towards sequences of the genes and proteins involved rather than fragments. Additionally, it can also be deduced that engagement of whole sequence is discouraged.

5. It is disclosed in this study that all AASs, but Kyte-Doolittle demonstrated highest interaction (100%) at the CFs when all the four mutations are engaged concomitant (Table 3 Row 8). The levels of interaction at the CFs by TAD and p53 demonstrated by simultaneous engagement of all mutants using Kyte-Doolittle are 82% and 97.0%, respectively. Engaging the mutants individually did not demonstrate consistent increased activities unlike when they are concurrently utilized. This appears to symbolize that associated oncological, hence biological characteristics arising from sequence changes requires concomitant engagement of all mutations, where there are more than one mutation.

6. The findings revealed that except for position 78 of the EIIP-based results of the analysis of p53, all other positions studied are the points of common interactions (Table 3, column 4). The result shows that all mutants did not yielded 100% rather 95.5%. However, an individual mutant, W23S provided 100% activity. This study therefore recommends that oncological examinations should focus on activities at the position of common interaction (CF).

7. All AASs excluding CHAM830107, KLEP840101, FAUJ880111 and FAUJ880112 demonstrated differences in the level of interactions at the positions of common interaction. ISM-based analysis of the sequences of both wild-type and the mutants showed same level of interaction (100%). This is as shown in table 3, Columns 7, 9, 10 and 11. It was observed that for these AASs, though there are sequence alterations, the AAS values did not change. This is because in these AASs, only two values (0 and 1) are involved and most have zero values. As a result, the AAS value of the amino acids belonging to the consensus and mutated sequences (L, Q, W, S, and F) involved in the four mutations is same (zero). As a result, there was no change in activity signifying insensitivity of the AASs. It is recommended that in the oncological evaluations, all AASs must be engaged to compliment these results.





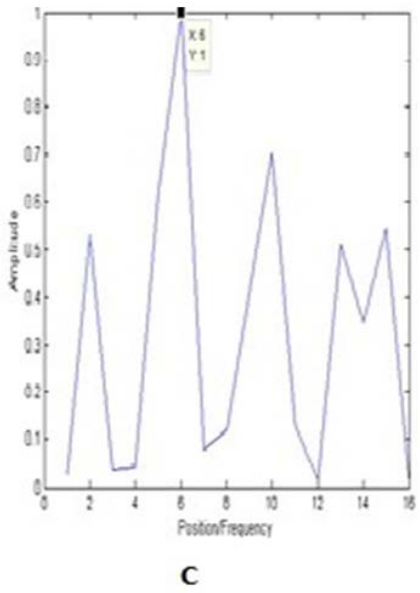


Figure 10: Showing the results of the Informational Spectra of (A) nDARC with amplitude 0.844 signifying 84.4% readiness for binding interaction with other bio-molecules and (B) mutant (nDARC Y41F) with amplitude of 1.00 hence 100% availability, and (C) the Common Informational Spectrum showing CF at position 6 (courtesy of [25,38]).

8. Similar assessment using the Plasmodial protein nDARC [25] provided similar results. Abrogation of pharmacological property of a plasmodial protein nDARC caused by a single mutation nDARC Y41F demonstrated a restoration 100% from decreased pharmacological activity (84.4%) (Figure 10). This appears to signify that this uncovered bio-functionalty applies to all proteins including oncogenes.

This study provides a guide for a computerized bioinformatics-based approach that may in future take over the assessment of oncological characteristics and help rationalize resources and time invested in preliminary and fruitful clinical cancer researches that had produced vast information on genetic variations (mutations) [49].

Conclusions

We preliminarily proposed multi-disciplinary centers where diseases need be rationally investigated, therapeutic interventions and biomedical devices designed using sequence information-based bioinformatics techniques. This novel computerized Informational Spectrum Method-based procedure requires simply, a Discrete Fourier Transform process, all Amino Acid Scales and protein sequences involved. As a robust, resource- and time-saving approach, it is envisaged to assist immeasurably, clinical investigations including oncological assessment.

In this study, protein residues of an oncogene, p53 and its motif, Transactivation Domain (TAD) are processed using ISM procedure and seven out of the 565 Amino Acid Scales. Several peaks were generated, each signaling a bio-functionality. The results revealed that the oncogene, p53 and the motif have different positions of interaction implying that neither the protein sequence of fragment (motif such as the TAD) nor the whole genome but only the protein involved in the interaction is appropriate for use in this computerized technique. The outcome also disclosed that complete reversal of the abrogation of activity by the mutants was achieved when all the mutants are concomitantly engaged. Additionally, consistency was observed at the position of common interaction rather than another chosen position indicating oncological assessment and others should make use of positions of common interaction.

This study, which is a demonstration of the employment of a Fourier Transform-based, Digital Signal Processing technique that has fetched reliable technologies like Radar, Image Processing and Speech Detectors in investigating the oncological properties of the Transactivation Domain of p53 serves a guide for future assessments of all biological functionalities including oncological properties.

Conflict of Interest

All the authors declared that they have no conflict of interest.

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