

The Effects of Temporomandibular Disorder on Collagen I and Fibronectin in Human Temporomandibular Joint Discs and Serum

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Introduction

The human temporomandibular joint (TMJ) is located between the mandibular condyle, the glenoid fossa of the temporal bone, and the articular eminence of the temporal bone (Almarza and Athanasiou, 2004) (see Figure 1). Both the condyle and temporal bone surface consist of dense cortical bone, and dense fibrous connective tissue covers both of these surfaces (Hayt et al., 2000). Furthermore, the TMJ is a modified hinge joint that allows open/close, forward/backward, and lateral movements (Temporomandibular Joint, 2006).

Located within the joint is a biconcave-shaped, fibrocartilaginous disc (Almarza and Athanasiou, 2004; Milam, 2003) (see Figure

1). The disc is avascular and does not contain nerves in the central area; however, nerves and vessels are located on the periphery of the disc (Hayt et al., 2000). The thinnest area of the disc is 1mm and is located in the middle

portion, while the periphery is usually thicker (2-3mm) (Hayt et al., 2000). The thin middle area allows the disc to alternate between a

concave and convex shape and allows the condyle to move in a circular motion (Detamore and Athanasiou, 2003a).

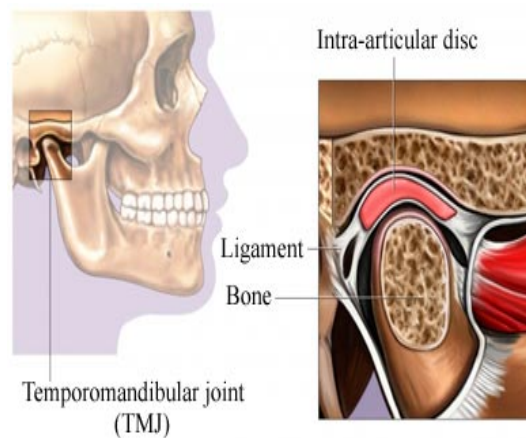


Figure 1: Figure of the TMJ, which is located between the mandibular condyle and fossa of the temporal bone. Located between within the joint is a fibrocartilage disc (Almarza and Athanasiou, 2004 and Milam, 2003).

The TMJ disc functions to increase the surface area for load distribution, provide shock absorbance, and assist with joint lubrication, which is provided by the synovium (Detamore and Athansiou, 2003a; Synovium, 2006). Because the TMJ is a modified hinge joint, the articulating surfaces must endure constant loading and is subjected to mastication (Temporomandibular Joint, 2006; Nakano and Scott, 1989). Therefore, the disc cushions the surrounding bones from continual shock. Furthermore, the disc reduces the impact of shock by increasing the surface area for load distribution. Additionally, the disc helps produce synovial fluid to lubricate the joint, which allows for easy joint movement (Synovium, 2006). Lastly, the disc separates the joint into different compartments that allow for various joint movements (Almarza and Athanasiou, 2005). Because the TMJ allows multidirectional movement (Temporomandibular Joint, 2006), the disc must consist of specialized components to bear constant loading.

Some components that constitute the TMJ disc are collagen types I, II, III, VI, IX, XII and extracellular matrix (ECM) components, such as fibronectin (FN) (Detamore and Athanasiou, 2003). Collagen is composed of three collagen peptide chains, called α chains (Alberts et al., 2002). These α chains wind around each other into a triple helical structure (Alberts et al., 2002). This collagen structure is resistant to proteolytic enzymes; however, degraded collagen is easily digested (Bank et al., 1997). Furthermore, the cross-linked structure of the collagen fibers provides the TMJ disc with structure and tensile resilience (Eyre, 2004; Almarza and Athanasiou, 2004).

Specifically, collagen I, or fibrillar collagen, is the most abundant collagen type found in the TMJ disc (Alberts et al., 2002; Almarza and Athanasiou, 2004). After collagen I is deposited into the ECM of the tissue, the collagen molecules form into polymers, called collagen fibrils (Alberts et al., 2002). Collagen fibrils then collect into bundles called collagen fibers (Alberts et al, 2002). According to Milam, Klebe, Triplett, and Herbert

(1991), collagen I is mostly concentrated in the anterior and posterior bands of human TMJ discs, and they exist in the mediolateral direction (as cited in Detamore and Athanasiou, 2003; Almarza and Athanasiou, 2004).

Furthermore, FN, or basal adhesion proteins, is found in either blood plasma or the ECM of cells and exists as a 250kDa dimer (Extracellular Matrix Components, n.d.; Pankov and Yamada, 2002). FN contains dual properties; the protein can either assist with wound healing or cartilage degradation (Pankov and Yamada, 2002; Homandberg, Wen, and Hui, 1998). For example, FN aides with wound healing by mediating cell adhesion, migration, growth, and differentiation (Pankov and Yamada, 2002). This protein consists of three subunits: 12 FI, two FII, and 15-17 FIII, which make up about 90% of the FN sequence (Pankov and Yamada, 2002). Because of alternative splicing of a single pre-mRNA, human FN can exist as 20 variations (Pankov and Yamada, 2002). Within FIII repeats, a main type of splicing occurs (Pankov and Yamada, 2002). As a result of exon usage or skipping, either EDB (or EIIIB) or EDA (or EIIIA) are included or excluded in the FN sequence (Pankov and Yamada, 2002).

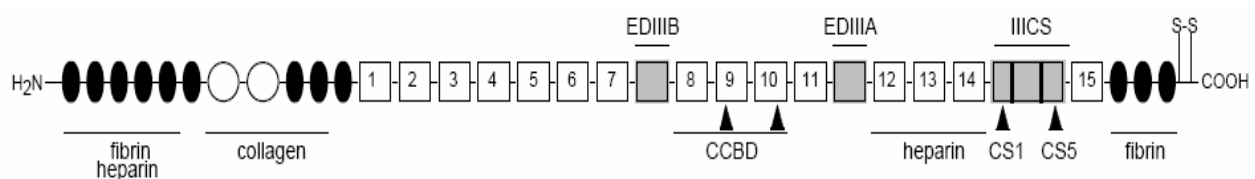


Figure 2: Figure shows the FN structure. The black ovals signify FI subunits, the white circles characterize FII subunits, and the squares indicate FIII subunits. Shaded squares represent the alternatively spliced regions, which include EDIIIB, EDIIIA, or IIICS domains. Cells bind to the following domains: the CCBD, which includes the synergy site (FIII₉) or the RGD domain (FIII₁₀), and the FIIICS, which includes CS1 and CS5 sites. Furthermore, other ECM components, such as fibrin, heparin, and collagen, bind to the indicated regions (Hotchin, Kidd, Altroff, and Mardon, 1999).

FN subunits have specific domains for the adhesion of cells, heparin, collagen, and fibrin (Hotchin et al., 1999) (see Figure 2). For instance, the central cell binding domain

(CCBD) is located at FIII₈₋₁₀ and allows the adhesion of a variety of cells (Hotchin et al., 1999). However, in the FIIICS region, the CS1 and CS5 domains allow only a small number of cells to bind to FN (Hotchin et al., 1999). The adhesion of cells to FN depends upon the type of integrin receptor, which is located on the surface of cells (Hotchin et al., 1999). Integrin receptors are heterodimers that contain two subunits: an α and β subunit (Hotchin et al., 1999). Most integrins, such as $\alpha 5\beta 1$ and $\alpha v\beta 3$, recognize a minimal recognition site of FN, called the RGD site (Hotchin et al., 1999). The RGD site consists of the Arg-Gly-Asp sequence in the FIII10 module (Wierzbicka-Patynowski and Schwarzbauer, 2003; Hotchin et al., 1999).

Additionally, FN contains two heparin-binding domains, which bind to heparin sulfate proteoglycans (Pankov and Yamada, 2002). In the C-terminal of FN, the strongest heparin-binding domain exists, while the N-terminal contains the weaker binding domain (Pankov and Yamada, 2002). The high-affinity domain also binds to glycosaminoglycans and chondroitin sulfates, while the N-terminal domain mediates FN interactions with bacteria (Pankov and Yamada, 2002).

Furthermore, FN binds to collagen in the FI₆₋₉ and FII_{1,2} repeats (Pankov and Yamada, 2002). These FN repeats bind more effectively to gelatin, or denatured collagen, rather than native collagen (Pankov and Yamada, 2002). Consequently, collagen may bind to FN through collagen unfolding (Pankov and Yamada, 2002). According to a previous study, triple helical collagen unfolds locally at body temperature (Leikina et al., 2002 as cited in Pankov and Yamada, 2002). This study suggests that the collagen-binding domain of FN may interact with native collagen in vivo (Pankov and Yamada, 2002).

Lastly, FN binds to fibrin through two fibrin-binding sites (Pankov and Yamada, 2002). The major fibrin-binding site is located in the N-terminal domain of FN, while the remaining fibrin site is located in the C-terminal (Pankov and Yamada, 2002). FN-fibrin

binding is significant because this adhesion allows cell binding or cell migration into fibrin clots (Pankov and Yamada, 2002). After an inflammatory response, FN-fibrin binding may also aid macrophage clearance of fibrin from circulation (Pankov and Yamada, 2002).

Although FN contains domains that allow tissue formation, Homandberg, Wen, and Hui (1998) state that FN fragments possess the ability to degrade cartilage (Homandberg, Meyers, and Xie, 1992). For example, native FN does not contain degrading properties; however, when FN is lysed, the FN fragments are able to induce tissue breakdown (Homandberg, Meyers, and Xie, 1992). Specifically, FN fragments have been shown to promote the gene expression of collagenase and stromelysin in synoviocytes and inhibit endothelial cell growth (Werb et al., 1989 as cited in Homandberg, Meyers, and Xie, 1992; Homandberg et al., 1985 as cited in Homandberg, Meyers, and Xie, 1992). In a study conducted by Homandberg, Meyers, and Xie (1992), FN fragments that contain the amino terminal 29- and 50-kDa gelatin-binding domain induced the production of proteinases in bovine articular cartilage. Furthermore, FN fragments are able to enter cartilage tissue and surround chondrocytes, and they are able to promote matrix metalloproteinase-3 levels (Xie and Homandberg, 1993 as cited in Homandberg, 2001; Xie et al., 1994 as cited in Homandberg, 2001). Although the TMJ disc contains a variety of components to help maintain the tissue, the disc is still susceptible to disease.

Temporomandibular disorder (TMD) affects approximately 10 million individuals in the U.S., and this disorder usually affects women in their child-bearing years (Blum, 2006; Temporomandibular Disorder, 2005). TMD is a disease of the TMJ, and according to L. George Upton, M.S., DDS from the University of Michigan Dental School, TMD is classified as the history of or current TMJ pain, clicking, locking, jaw muscle pain or abnormal disc

position (Upton, n.d.). According to the National Institute of Dental and Craniofacial Research, other symptoms of TMD include face, neck, and shoulder pain (National Institute, n.d.). Furthermore, headaches, dizziness, and earaches may be related to TMD (National Institute, n.d.). In severe cases of TMD, the TMJ disc may dislocate, causing either an open-mouth or close-mouth position (Detamore and Athanasiou, 2003). Specifically, an open-mouth position is caused by a nonreducing displacement of the mandibular condyle in front of and above the articular eminence (Nitzan, 2002). Currently, research is being conducted to further understand how TMD affects the composition of the TMJ disc and how tissue remodeling may induce TMD.

Both FN and collagen I of the TMJ disc are affected by TMJ disease. A study conducted by Leonardi, Michelotti, Farella, Caltabiano, and Lanzafame (2004) discovered that patients with deranged TMJ discs contained strong FN expression, while weak FN expression was present in healthy TMJ discs. In addition to FN, collagen I is shown to be affected by disease. In the late stage of osteoarthritis, TMJ discs contain a reduced and disorganized collagen network (Dijkgraaf, DeBont, Boering, and Liem, 1995). Although this research reflects histological changes in diseased TMJ discs, further research is needed to completely understand the effects of TMD on the TMJ disc and how tissue remodeling affects TMD.

Because of the limited knowledge regarding the effects of TMD on collagen I and FN, this study was conducted to determine the effects of TMD on collagen I and FN in human TMJ discs and serum. Based on the previous literature, the hypothesis for this study is that TMJ discs and serum of patients with TMD will contain an increased amount of FN and decreased amount of collagen I.

Morphology

Materials/Methods

Samples

All human TMJ discs and serum were collected by L. George Upton, M.S., DDS from the University of Michigan Dental School. Prior to collection, subjects who donated samples signed a consent form that was reviewed by the Institutional Review Board (IRB) at the University of Michigan. The IRB also reviewed the protocol that allowed the removal of human TMJ serum and discs. Subjects who donated patient samples were symptomatic for TMD, while subjects who donated control samples were asymptomatic for TMD. Control subjects were also treated for unrelated conditions. Using an enzyme-linked immunosorbent assay (ELISA), the collagen I and FN concentrations were analyzed in human TMJ serum. Thirteen TMJ serum samples from 9 different subjects were assessed, and 7 serum samples were considered control. Additionally, hematoxylin and eosin (H&E) and fluorescent stains were used to immunohistochemically analyze human TMJ discs. Fifteen human diseased TMJ discs from 11 subjects were analyzed. Joseph R. Natiella, DDS created two assessment scales that allowed the TMJ discs to be categorized according to the 1.) severity of morphological damage (see Table 1) and 2.) intensity of fluorescence (see Table 2). For both categories, the scale ranged from 1 (least severe) to 3 (most severe).

| Level

Characteristics

|

I	Multidirectional fiber bundles. Architecture: cross and longitudinal fiber bundle orientation. Preservation of evenly dispersed fibrocytes.
II	Areas of hyalinization. Foci of prechondrocytes in zones of hyalinization. Some preservation of multidirectional fiber bundles.
III	Generalized hyalinization. Multiple foci of cartilage. Normal architecture almost totally obliterated. Fragmentation and clefting in multiple foci.

Table 1: Table displays the classification used to assess the morphological damage and intensity of fluorescence in diseased human TMJ discs.

Fluorescent Staining	
Level	Characteristics
I	+++ collagen I - fibronectin
II	+ collagen I + fibronectin
III	- collagen I ++ fibronectin

Table 2: Table shows the classification system used to determine FN and collagen I expression in diseased human TMJ discs.

Results

ELISA
Collagen I

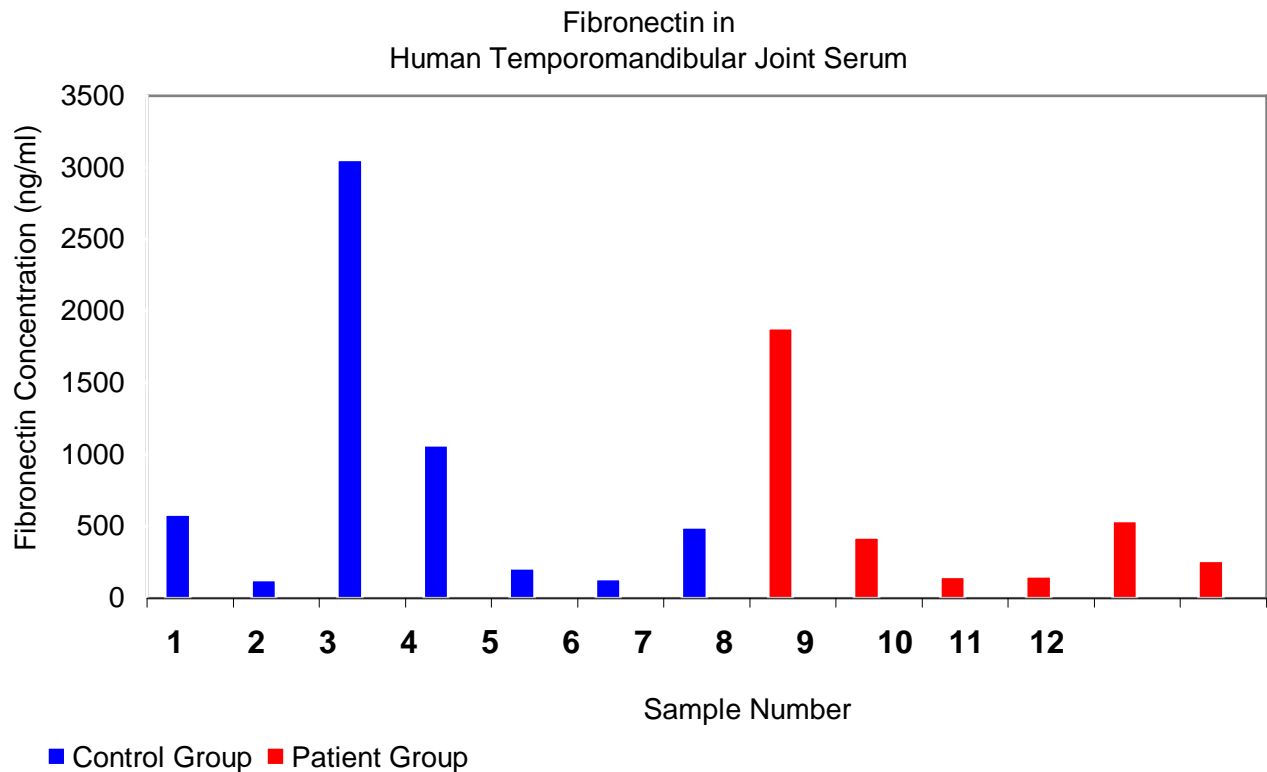
I will redo this experiment, and then I will add the results to my paper.

FN

The FN concentrations do not express a clear pattern in both the control and patient human TMJ serum samples (see Table 3 and Graph 1). In the control samples, FN concentrations ranged from 126.328ng/ml to 3053.606ng/ml, and the patient sample FN concentrations ranged from 147.352ng/ml to 1883.007ng/ml (see Table 3). Furthermore, FN concentrations do not express a clear pattern in both the right and left TMJ serum from control and patient samples (see Table 4 and Graph 2). For instance, control patient number 2 contains 3053.606ng/ml of FN in the right TMJ and 1063.690ng/ml of FN in the left TMJ (see Table 4). Additionally, sample patient number 3 contains 260.059ng/ml of FN in the right TMJ and 1883.007ng/ml of FN in the left TMJ (see Table 4). Lastly, the corresponding FN concentrations, disc morphology, collagen I fluorescence, and FN fluorescence are shown in table 5.

Fibronectin in Human Temporomandibular Joint Serum		
Sample Number	Fibronectin Concentration (ng/ml)	Control or Patient Sample
1	581.229	Control
2	126.328	Control
3	3053.606	Control
4	1063.690	Control
5	206.325	Control
6	135.298	Control
7	492.745	Control
8	1883.007	Patient Sample
9	422.949	Patient Sample
10	147.354	Patient Sample
11	152.796	Patient Sample
12	538.098	Patient Sample
13	260.0585	Patient Sample

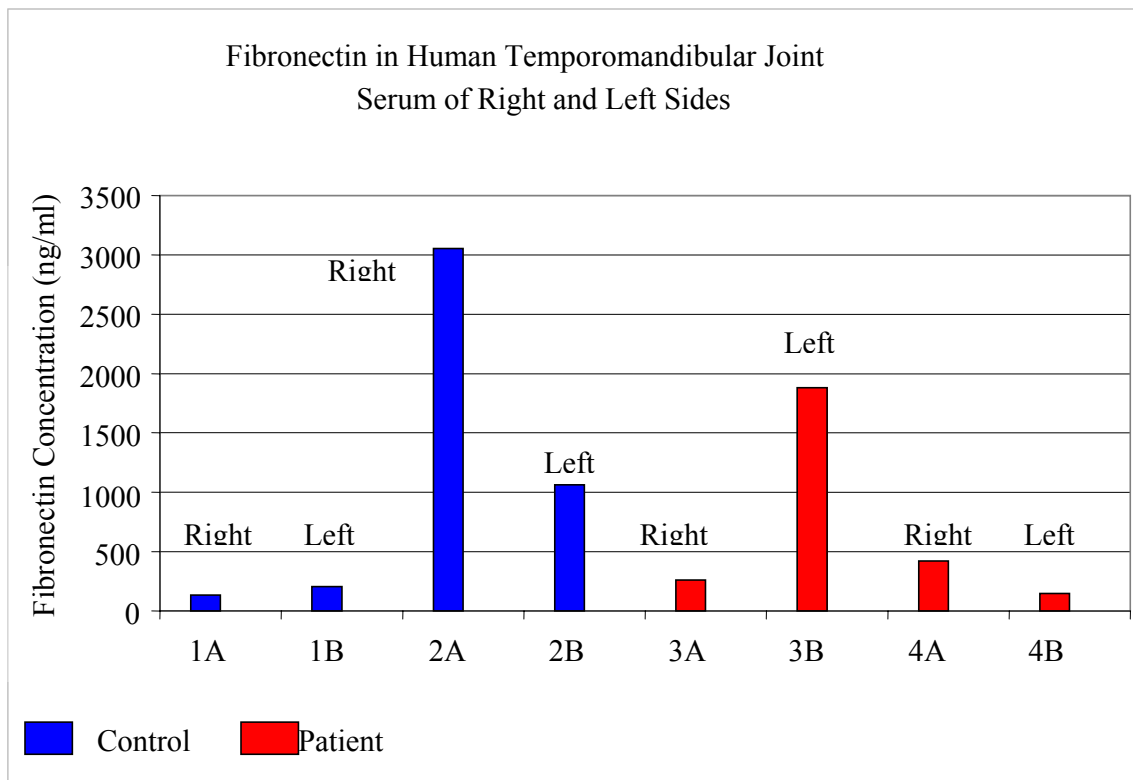
Table 3: The table displays the FN concentration (ng/ml) in human control and patient TMJ samples. The FN concentrations were analyzed with ELISA.



Graph 1: The graph displays the concentration of FN (ng/ml) in both control and patient human TMJ serum samples.

Fibronectin in Human Temporomandibular Joint Serum of Right and Left Sides				
Sample Number	Fibronectin Concentration (ng/ml)	Control or Patient Sample	Right or Left Side	
1A	135.298	Control	Right	
1B	206.325	Control	Left	
2A	3053.606	Control	Right	
2B	1063.690	Control	Left	
3A	260.059	Patient Sample	Right	
3B	1883.007	Patient Sample	Left	
4A	422.949	Patient Sample	Right	
4B	147.354	Patient Sample	Left	

Table 4: The table displays the FN concentrations (ng/ml) in both control and patient human TMJ serum samples of four patients. Each patient donated a serum sample from both their right and left TMJ.



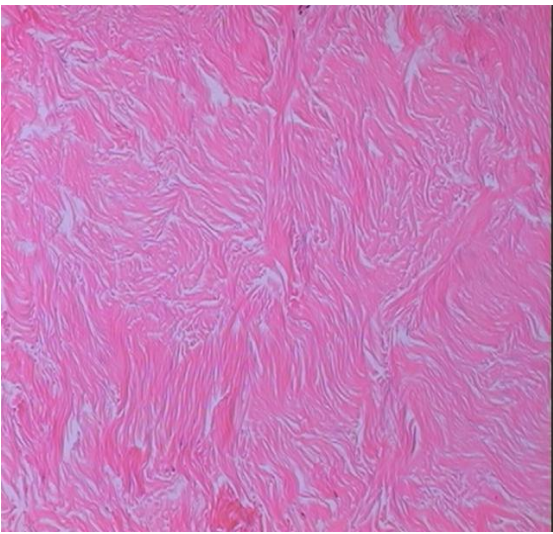
Graph 2: The graph displays the FN concentrations (ng/ml) in right and left TMJ serum from both control and sample patients.

Sample #	FN Concentrations (ng/ml)	H&E	Collagen I Fluorescent Staining	FN Fluorescent Staining
1	581.228	None	None	None
2	126.328	None	None	None
3	3053.606	None	None	None
4	1063.690	None	None	None
5	206.325	None	None	None
6	135.298	None	None	None
7	492.745	None	None	None
8	1883.007	None	None	None
9	422.948	III	No picture	II
9	N/A	Non-diagnostic	N/A	N/A
10	147.354	None	None	None
11	152.796	II	No picture	No picture
12	538.097	II	II	No picture
13	260.058	III	No picture	No picture
13	N/A	N/A	N/A	No picture

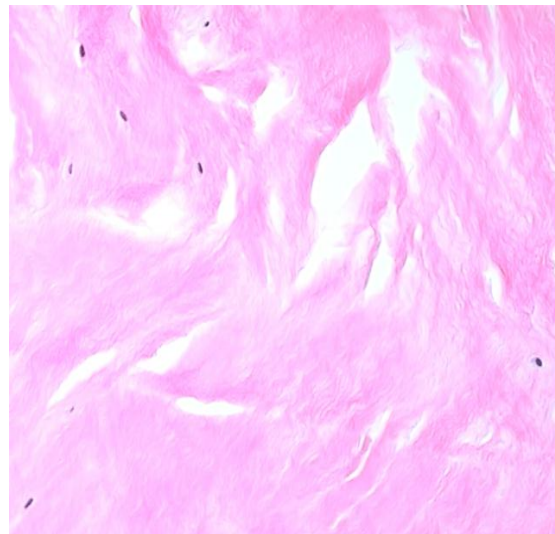
Table 5: The table displays the results of the H&E, collagen I fluorescent, and FN fluorescent staining of the human TMJ discs and, in some instances, the corresponding FN concentration (ng/ml) in the human TMJ serum samples. Serum Samples 1-8 did not have corresponding TMJ discs. However, serum samples 9-13 had corresponding TMJ discs. Also, in some cases, a disc was viewed in more than one location; therefore, some discs contain more than one classification for either H&E, collagen I fluorescent, or FN fluorescent staining. Lastly, some discs contained weak expression of either collagen I or FN. As a result, the disc fluorescence could not be classified; this circumstance is indicated by “No picture”.

H&E

In the left TMJ disc, sample 8 expressed normal collagen bundle arrangement and acellular tissue at 10X magnification (see Slide 1). Slide 1 tissue morphology is classified between a level I and II (see Slide 1). In slide 2, the right TMJ disc of sample 9 displayed hyalinized and clefted tissue at 10X magnification (see Slide 2). Also, the disc contained a few fibroblasts, and the tissue morphology is classified as a level III. Lastly, the morphology of all 15 human TMJ discs is presented in table 6.



Slide 1: H&E stain of left diseased disc from sample 8. Slide shows typical collagen I bundles, and slide is acellular (10X magnification). This disc morphology is classified between a level I and II.

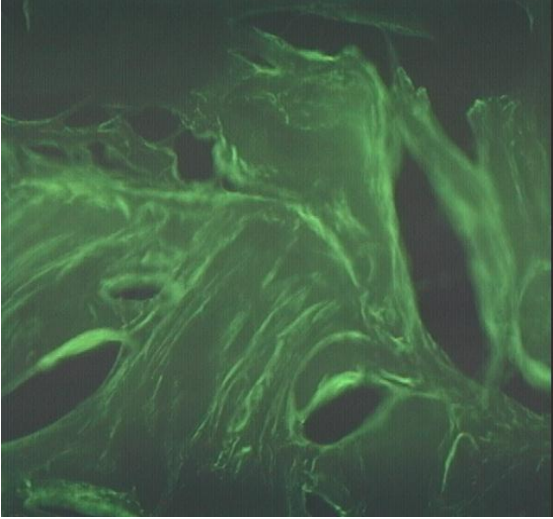


Slide 2: H&E stain of right diseased TMJ disc from sample 9, which belonged to the patient who also donated sample disc 8. Slide shows hyalinization, clefting, and fibroblasts (10X magnification). The disc morphology is classified as a level III.

*Fluorescent Stain**FN*

At 10X magnification, sample 8 expressed a level III of fluorescent staining, which included a strong FN expression and weak collagen fibril expression (see Slide 2 and Slide 3). Furthermore, FN was weakly expressed in blood vessels of sample 12 at 10X

magnification (see Slide 4). Lastly, the FN fluorescence of all 15 human TMJ discs is presented in table 6.



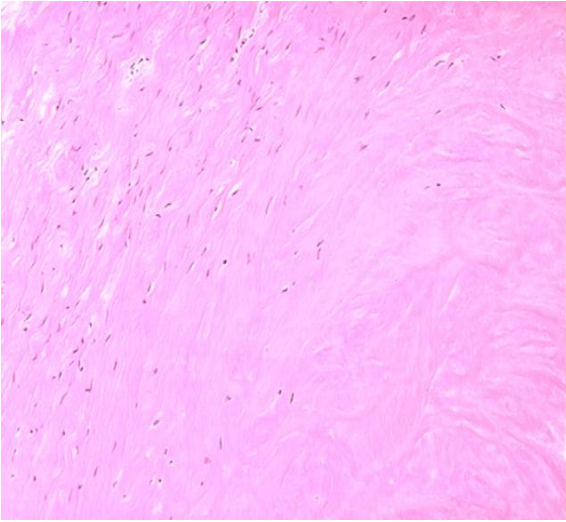
Slide 3: Fluorescent stain of FN in right diseased TMJ disc from sample 8. Slide shows clefting (10X magnification). The fluorescent staining of this disc is classified as a level III, which includes strong FN expression and weak collagen fibril expression (see Slide 2).



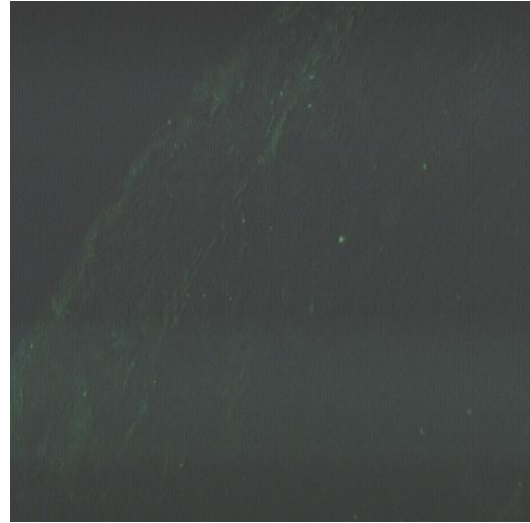
Slide 4: Fluorescent stain of FN in diseased human TMJ disc of sample 12. FN is located within a blood vessel (10X magnification). The FN staining of this disc is considered a level II/III.

Collagen I

Additionally, in the right TMJ disc of sample 5, collagen I fluoresced in correlation with fibroblasts (see Slide 5 and Slide 6). Both slides 5 and 6 were observed at 10X magnification. Also, the collagen I fluorescence of all 15 human TMJ discs is displayed in table 6.



Slide 5: H&E stain of right diseased TMJ disc from sample 5. Upper half shows fibroblasts and hyalinization, while lower half is acellular (10X magnification). The morphology of this disc is classified as a level II.



Slide 6: Flourescent stain of collagen I in TMJ disc of sample 5. Upper half expresses collagen I, while lower half does not display collagen I (10X magnification). The collagen I expression of this disc is classified as a level II.

Disc From Sample #	H&E Classification	Collagen I Fluorescent Staining	FN Fluorescent Staining
1	III	No picture	II
2	Non-diagnostic	N/A	N/A
3	None	None	None
4	II	No picture	No picture
5	II	II	No picture
6	III	No picture	No picture
7	N/A	N/A	No picture
8	I or II	II or III	III
9	III	III	N/A
10	III	I or II	No picture
11	I	II	II
12	III	III	II or III
13	II-III	N/A	N/A
14	III	No picture	No picture
15	III	N/A	N/A

Table 6: The table displays all 15 human TMJ disc samples and the corresponding H&E, collagen I fluorescent, and FN fluorescent staining results. Some discs contained weak expression of either collagen I or FN. As a result, the disc fluorescence could not be classified; this circumstance is indicated by “No picture”.

Discussion

In human TMJ serum of both sample and control patients, FN did not express a definitive pattern. Control samples displayed FN concentrations of 126.328ng/ml to 3053.606ng/ml, while the patient samples displayed a FN range from 147.352ng/ml to 1883.007ng/ml (see Table 3). Not only does this data not support the hypothesis that FN concentrations increase in diseased human TMJ serum, but the findings are not consistent with previous studies. For example, when compared to healthy human TMJ discs, FN expression increased in deranged TMJ discs (Leonardi et al., 2004). Furthermore, elevated amounts of FN were found in the synovial fluid of knee joints from patients with rheumatoid arthritis (Griffiths, Herbert, Perrett, and Scott 1989 as cited in Xie, Meyers, and Homandberg, 1992). Lastly, a study conducted by Carnemolla, et al. (1984) demonstrates that FN increased in synovial fluid from patients with rheumatoid arthritis and osteoarthritis (as cited in Homandberg, Wen, and Hui 1998). Despite the discrepancy, the FN data may show a particular stage of tissue remodeling.

Because FN aides with tissue remodeling and degradation, the FN data may reflect FN's contribution to the tissue repair process of each sample. For example, FN contains the RGD sequence and synergy site (Alberts et al., 2002) (see Figure 2) that bind to $\alpha 5\beta 1$ integrin receptors of cells (Wierzbicka-Patynowski and Schwarzbauer, 2003). This integrin receptor also binds to the N-terminal end of FN fragments, which include either the FI_{1,9} or FII_{1,2} subunits (Pankov and Yamada, 2002). As a result of the FN-integrin binding, cell adhesion and, thus, tissue formation occur (Alberts et al., 2002). Furthermore, FN mediates fibroblast migration and allows fibroblasts to adhere to fibrin (Grinnel 1984 as cited in Aota et al., 2005). Consequently, this aides cells with organizing collagen and, hence, promotes tissue formation (Grinnel, 1984 as cited in Aota et al., 2005). However, unlike native FN, FN

fragments contain degrading properties (Homandberg, Meyers, and Xie, 1992). For example, in synoviocytes, FN can activate the gene expression of collagenase and stromelysin (Werb et al., 1989 as cited in Homandberg, Meyers, and Xie, 1992). Furthermore, FN fragments degraded bovine articular cartilage by either suppressing the proteoglycan synthesis or inducing the production of matrix metalloproteinases (MMP) (Homandberg, Meyers, and Xie, 1992). Therefore, because FN's involvement with tissue formation varies, the FN data may reflect FN's specific contribution to each sample. Perhaps decreased levels of FN indicate that the disc is remodeling to a functional state, while increased FN levels indicate the presence of cartilage degrading FN fragments. However the collagen I ELISA results are needed to support this statement. Once the collagen I data is collected, the relationship between the FN and collagen I can be determined for each sample. For instance, a sample containing high FN levels and low collagen I levels may indicate the presence of degrading FN fragments. Because EDA-positive FN fragments induce MMP-I, which breaks down collagen I (Saito et al., 1999; Eyre, 2004), this particular FN fragment may be found in samples containing low collagen I levels.

Furthermore, FN concentrations do not express a clear pattern in both the right and left TMJ serum from control and patient samples (see Table 4 and Graph 2). For instance, control patient number 2 contains 3053.606ng/ml of FN in the right TMJ and 1063.690ng/ml of FN in the left TMJ (see Table 4). Additionally, sample patient number 3 contains 260.059ng/ml of FN in the right TMJ and 1883.007ng/ml of FN in the left TMJ (see Table 4). The varying amounts of FN in each patient's right and left TMJs may reflect the patient's dominant chewing side (Almarza and Athanasiou, 2004). For example, a possible cause of TMD is increased pressure on the TMJ (Temporomandibular Disorder, 2005). A dominant chewing side will increase pressure on the TMJ, thus, possibly increasing the rate of TMD formation. As a result of TMD, increased FN may be observed (Leonardi et al., 2004).

Therefore, an increased FN concentration in a one TMJ side may indicate increased use of that joint.

Additionally, the FN fluorescent staining demonstrates that FN is expressed in both the ECM and blood plasma of diseased human TMJ discs. For example, Slide 3 displays FN expression surrounding the clefted regions of sample 8 (see Slide 3). To confirm the location of the disc area observed, the fluorescently stained slide was compared with Slide 2, which showed the disc morphology. In Slide 2, clefting was also shown. This data confirms that FN is present in the ECM of the human TMJ disc (Milam, Klebe, Triplett, and Herbert, 1991 as cited in Detamore and Athanasiou, 2003a) and demonstrates that FN is not located in TMJ clefts.

Furthermore, the fluorescent staining of the TMJ disc in sample 12 showed FN in blood vessels (see Slide 4). This data confirms that FN is found in blood plasma (Pankov and Yamada, 2002). Perhaps the presence of FN in the blood vessel indicates that FN travels through the blood to the damaged TMJ disc. This would allow the FN concentration to increase in the damaged area. Increased FN may reflect an attempt to repair the damaged tissue or aide with cartilage degradation. Further studies are needed to determine the exact mechanism of FN's involvement of TMJ disc repair.

Lastly, the TMJ disc of sample 5 revealed a correlation between collagen I expression and the presence of fibroblasts (see Slide 5 and Slide 6). This data confirms that fibroblasts secrete matrix molecules, such as collagen, to maintain the ECM (Alberts et al., 2002). Perhaps the presence of fibroblasts in correlation with collagen I indicate the tissue's attempt to repair itself. However, future analysis of the characteristics of diseased TMJ tissue is needed to confirm this statement.

Future Studies

To accurately determine FN's contribution to diseased TMJ discs, the amount of collagen I in control and diseased human TMJ serum is needed. This data will allow the relationship between FN and collagen I to be determined. If the data indicates that FN induces the degradation of collagen I, then the TMJ serum can be probed for cartilage-degrading FN fragments. To confirm the degrading properties of these fragments, the FN fragments can be incubated with collagen I. After incubation, the amount of collagen I remaining will determine the degrading properties of FN fragments.

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Lindsay just graduated from Daemen College with a bachelor's degree in Biology. Her senior thesis was the study of the effects of osteoarthritis on collagen I and fibronectin in human temporomandibular joint disks. In addition to her senior research, Lindsay participated in the Research Experience for Undergraduates (REU)

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