Informationisation construction of pharmacology continuing education – a case study on big data analysis of the aetiology of rheumatoid arthritis

Qun Chen¹, Jie Wang¹,†, Faris Kateb², Radwan Kharabsheh³

¹ College of Pharmacy of Bozhou Vocational and Technical College, Bozhou 236800, China
² Department of Information Technology, Faculty of Computing and Information Technology, King Abdulaziz University, Jeddah, Saudi Arabia
³ Applied Sciences University, Al Hidd Bahrain

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Abstract
The goal of promoting Information and Communication Technology of continuing education in colleges and universities is to standardise the process of teaching and scientific research, make the process more scientific and refined, so as to facilitate and improve the quality of teaching and scientific research, as well as professional disciplines. Rheumatoid arthritis is a disease with chronic, symmetrical and non-specific inflammation of the synovium of the joints (subcutaneous nodules, pericarditis, pleurisy, pneumonia, peripheral neuritis etc.) as the main clinical manifestations. The analysis of pharmacological big data information helps to understand its aetiology and pathological mechanism, which is complex and involves various pathogenic factors.

Keywords: continuing education, ICT, rheumatoid arthritis, big data analysis, pathogenesis

1 Introduction

It is imperative to actively promote information and communications technology (ICT) application to education and education and teaching reform in colleges and universities, and carry out in-depth integration. The intelligent model based on big data can analyse and process education-wise data, provide summary and prediction of educational decision-making and discover new characteristics and new regulations of learning and teaching, in such a way as leads to improvement in the level of scientific decision-making in education and provide an important reference for advancing education and teaching reform. According to pharmacology, rheumatoid arthritis (RA) is a disease with immune abnormalities. At present, the pathogenesis is not fully understood.

† Corresponding author.
Email address: 467204461@qq.com
It is related to genetic factors and environmental factors. Immune disorders are the main process of disease, during which one’s own immune cells are immune to one’s own synovial tissue. The cell factor is related to the clinical symptoms and blood sedimentation. C-reactive protein is elevated, the immune cells secrete related immune globulin – which are also rheumatoid factor – and CCP antibodies can be discovered. In addition, the informatisation platform of continuing education and the big data analysis of pharmacology major can be used to better conduct teaching and scientific research (see Table 1).

| Indicators          | RF   | ASO test | ESR   | C- CRP | CCP antibodies |
|---------------------|------|----------|-------|--------|----------------|
| Reference value     | Negative | <500 U | 0–15 mm/h | <8 mg/L | <5 RU/m        |

2 The construction of continuing education platform

The construction of continuing education platform is an important part of ICT development [1], which is composed of information curriculum resources, software application system and hardware system to provide services [2]. In the process of developing an ICT-based system for continuing education, first of all, we shall strengthen the construction of information management hardware facilities, which is mainly reflected in the construction of computers and a multimedia online teaching management platform that combines continuing education and online teaching. An ICP application platform for continuing education in universities [3] is a comprehensive business platform, which mainly includes a portal system, R&D of a network course platform and network resource management platform, an online teaching platform, a mobile app teaching platform, a teaching and administration management platform of various forms of continuing education (adult education, the self-study exam, distance education, open education and educational training), as well as other supporting platforms. Colleges and universities should build an Internet teaching and management platform, where ICT and teaching are deeply integrated [4].

3 The role of protein lyase

The abnormality of some proteases in RA has attracted much attention. At present, it is believed that the abnormal function of some proteases is related to the pathogenesis of RA. Cycle-dependent kinases (CDKs) play an important role in cell cycle regulation, and their inhibitory proteins (CDKIs) can inhibit cell cycle transformation. CDKI includes protein 16 (P16), egg from 21 (P21) and other components. P16 can inhibit the proliferation of RA synovium cells. The introduction of P16 gene into the MOUSE RA model with adenovirus vector can reduce the infiltration of lymphocytes and prevent the destruction of bone and cartilage, suggesting that p16 may become a new target in the treatment of RA. By observing the effect of genistein, an ATK inhibitor, on the growth of RA fibroblasts (FLS) under the action of cytokines, it was suggested that ATK plays an important role in dysplasia and transformation of RAFLS cells induced by IL-1, TNF-A and epidermal growth factors (EGFs). By comparing the expression of calpain mRNA and calpastatin mRNA in RA and A-type synovium cells and analysing the detection of calpastatin epitopes, it was shown that calpain and calpastatin systems were involved in the development of RA. Calpastatin can bind to autoantibodies in the serum of patients with RA, leading to inhibitory dysfunction. The increase in the level of calpain plays an important role in the degradation of connective tissue matrix and the destruction of RA cartilage. Calcium-dependent neutral protease inhibitors may provide new ideas for the treatment of RA. The abnormal activity of protein kinase A (PKA) in RA patients may...
be related to the inhibition of the common epitope of HLA IDRB, while the abnormal PKA signalling pathway in RA patients with DRB1*0401/*0402 is related to the common epitope of QK/RRAA [5].

The damage of normal structure and function of joints is the main feature of chronic inflammatory arthritis. In RA, the excessive proliferation of synovial lining cells and a large number of inflammatory infiltrations leads to pannus formation. This eventually causes damage to the articular cartilage and bone, which is believed to be due to excessive proliferation of synovial cells and secretion of a large number of protein lyases. There are four types of protein lyases involved in matrix degradation: (1) metalloproteinases (gelatinase, collagenase); (2) cystine proteases (such as cathepsin B, D, H, L); (3) aspartic acid protease (e.g., cathepsin D) and (4) serine proteases (such as plasminogen activators and their activated products plasminogen). Serine proteases and metalloproteinases are the most studied. Urokinase-type plasminogen activator, which belongs to serine protease family, plays an important role in the degradation of the articular cartilage and bone matrix [6].

TPA is a single chain glycoprotein synthesised and secreted by vascular endothelial cells. It consists of 527 amino acid residues with a molecular weight of 70,000. It mainly plays a physiological thrombolytic role in blood vessels. Under certain conditions, UPA mainly acts on physiology and pathology cell migration and tissue repair, which can mediate the degradation of pericellular matrix proteins. It can not only activate other proteases (such as plasminogen) but also directly degrade extracellular matrix and basement membrane itself [7].

Human uPA gene, located in the long arm of chromosome 10, is composed of 11 exons and can be transcribed into mature mRNA of 2.4 kH. When secreted for the first time, uPA is an inactive single-stranded, highly glycinated protein with a molecular weight of 55,000. When Lys158 is cleaved, it becomes an active double-stranded uPA linked by disulphide bonds, i.e. A 20 KDa and B 34 KDa. The A chain consists of I-158 amino acid residues, including two functional areas and one connective area, the epithelial growth factor functional area (1–49 amino acids), which binds to the region I of the uPA receptor (uPAR). The function of the annular region, also known as the Kringle region (50–131 amino acids), is unclear: a connective region consists of 132–158 amino acids and is located between the annular region and the silk helinase functional region. The B-chain is the serine protease cleavage zone, consisting of 159–411 amino acids, and it is the active centre of this enzyme [8].

In vitro, studies have found that the uPA in normal RA and osteoarthritis (OA, inflammatory arthropathy of cartilage, synovial membrane, expressed in synovial fluid and plasma, such as the synovial FLS, cartilage cells, the monocyte/macrophage). Polymorphic nuclear white blood cells and endothelial cells can synthesise the uPA, but expressions were significantly higher than normal. This may be related to the fact that RA in many ways is similar to the limited growth of the invasive tumour: synovial cell hyperplasia and a large number of lymphocyte infiltrations can form pannus. Between cells there is no contact inhibition, and pannus invades adjacent cartilage and bone tissue, eventually leading to cartilage and bone tissue damage. The damage to the cartilage and bone tissue relies mainly on the uPA-mediated degradation of the extracellular matrix.

Enzyme-linked immunosorbent assay (ELISA) and Northern blot were used to detect the antigen activity, content and mRNA expression level of uPA in the RA cartilage, which were significantly higher than those in OA and normal cartilage tissues. These results suggest that the degradation of matrix components in the RA cartilage may be closely related to the high expression of uPA protein and mRNA.

4 The action of free radicals

Nitric oxide (NO) is catalysed by NO synthase (NOS), and it can mediate and regulate various pathological processes. Induction of N0 in chondrocytes by interleukin-I (IL-I) or endotoxin provided the earliest evidence of involvement of NO in cartilage metabolism. Nitrite (NO-2), a large number of NO metabolites, was detected in the synovial fluid and serum of patients with RA and OA in 1992, which resulted in the speculation that NO may be involved in the pathological process of joint inflammation of these two diseases. Later many scholars confirmed that NO is an important inflammatory mediator in the pathogenesis of arthritis, thus promoting the in-depth study of the relationship between NO and inflammatory joint diseases.

The NOS inhibitor can reduce the urinary NO-2 pathological changes such as foot swelling, ankle synovitis
and cartilage damage. A dynamic comparison of the relationship between the degree of onset of AA rats and collagen-induced arthritis (CIA) rats and the amount of NO-3 excreted in the bodies of these two groups revealed that the peak time of the onset of arthritis and the content of NO- the urine of AA rats was significantly higher than those of CIA rats, and the expression level of induced NOS (iNOS) mRNA in the joints, liver and spleen of AA rats was significantly higher than that of CIA rats. The results indicate that the role of NO in the two arthritis models is different, and the excretion of NO-2/no- urine and the expression of iNOS mRNA in peritoneal macrophages are significantly increased. INOS gene knock-out mice showed reduced sensitivity of the inflammatory response induced by caraway glue. Injection of NO donor sodium nitroprusside (SNP) into the knee cavity of the rats not only caused knee swelling but also caused synovitis and other pathological changes.

5 Study on tyrosine kinase signal transduction system in synovial cells of RA

The detailed cellular signalling pathways in RA are not fully understood. Although the signalling pathways from different stimulators may not be identical, activation of growth factor receptor kinase (GFR) is considered to be the primary condition.

It was reported that the activity of tyrosine kinase and the expression of c-FOS and C-MYC in synovial cells of RA patients were significantly higher than those of OA patients. Tyrosine kinase antibody and tyrosine kinase inhibitor can significantly reduce the degree of RA arthritis. EGF, PDGF and FGF have been widely studied in RA.

EGFs, a 53-amino acid polypeptide, can induce the proliferation of synovial cells and blood vessels. Immunohistochemical results showed that the expression level of EGF in RA synovial lining cells was positively correlated with the thickness of the lining layer and the degree of neovascularature, which was significantly higher than that of OA and traumatic arthritis. There was no significant correlation between the expression level of EGF and the degree of mononuclear cell infiltration. Electron microscopy showed that an EGF was located on the rough endoplasmic reticulum of type B synovial cells and the surface of Golgi body and type A cells, suggesting that type B cells could activate type A cells.

PDGF is produced by synovial tissue with the stimulation of the anchored dependent growth of synovial cells and the formation of cell colonies. The experiment confirmed that PDGF can activate SRC family, such as PP60src, P59fyn and PP62yes. Immunohistochemistry showed that PDGF, phosphorylated tyrosine and FGF were expressed simultaneously in the synovium tissue, and the high level of phosphorylated tyrosine was positively correlated with inflammatory activity. In 1996, stimulation of synovial cells cultured in vitro with PDGF rapidly induced tyrosine phosphorylation and activation of MAPK, 70,000-s6 kinase (P70s6k) and 90,000-s6 kinase (P90rsk). Macrolide rapamycin completely inhibited the growth and P70s6k activation of synovial cells in vitro, but it did not affect the activation of tyrosine phosphorylation, MAPK or P90rsk. P90rsk is the downstream substrate of MAPK, and its kinase activity is regulated by MAPK. P70s6k and MAP kinase/P90rsk are two different pathways in the signal transduction of PDGF stimulation. The results showed that P70s6k, one of the S6 kinases mediated by growth factors, was closely related to the growth of synovial cells. PDGF passes through the signal transduction pathway of S6 kinase. It eventually induces the overexpression of proto-oncogenes C-FOS and C-MYC mRNA, which can stimulate the proliferation of synovium cells and aggravate joint destruction.

B-FGF was detected in the superplasm of synovial cells cultured in vitro. In 1994, it was demonstrated that the FGF stimulates synovial hyperplasia and neovascularisation in RA by autocrine and/or paracrine factors and that the expression level in RA is positively correlated with inflammatory activity, but it was hardly expressed in the OA synovial membrane [9].
6 Ion channels

Receptors, G-proteins and ion channels are membrane-bound proteins, so the easiest way to regulate ion channels is to interact directly with them through G-proteins. Activation of GIRK in the heart and brain and inhibition of N type and P/Q calcium channels have been demonstrated in this manner, and $\gamma \beta G$ is the G-protein-binding activator for these G-protein-sensitive ion channels.

Among these G-protein-regulated ion channels, K+ selective ion channels (IKACH) have been studied most clearly. In the heart, IKACH is a heteropolymer composed of GIRK and CIR, and it is usually induced by acetylcholine activation. IKACH is also present in the brain and is made up of GIRK. Several laboratories have found that GTP can activate IKACH and that $\gamma \beta G$ directly can activate IKACH. First, the effect of $\gamma \beta G$ on the effector demonstrated that $\gamma \beta G$ activated the channel 1000 times more than the effect of Ach or $\gamma \beta G$ applied outside the cell membrane. Although there were other opinions over the following years, it has been demonstrated in many laboratories that $\gamma \beta G$ is a direct activator of IKACH, binding to the N-terminal or C-terminal regions in GIRKs cells and directly activating them (21). At least eight AC isomers are regulated by $\gamma \beta G$, Ca2+ and phosphorylation. $\gamma \beta G$ can inhibit AC-I, AC and AC-V-VI. $\gamma \beta G$ can also be used with $\alpha Gs$ synergistic activation AC-II, AC-IV and AC-VII cells, if the $\alpha Gs$ and G-protein coupled receptors are activated at the same time, this usually does not affect the AC receptor (such as the Gi/0 and G coupling receptor $\alpha Q/11$) as long as it can release $\gamma \beta G$ that can produce cAMP. Therefore, the activation of these enzymes can be used as an indicator of simultaneous activation of several signal transduction pathways. AC with $\gamma \beta G$ combining site is not very clear, AC-Iby $\gamma \beta G$ site Cla areas might be located in the enzyme inhibition.

7 Conclusion

The pathogenesis of RA is not clear. Currently, we believe that RA is an autoimmune disease in which the initiating factor is not clear. It is speculated that the infection factor (such as viruses, mycoplasma or bacteria entering the body and its ingredients, such as sugar or sugar peptide fragments) is absorbed by the intra-articular synovial cells and the combination in synovial cells causes synthesis of proteoglycan, which changes the structure and antigenicity. Clinical studies believe that the disease is mostly related to the autoimmune system. Due to bacteria, viruses and the change of temperature after stimulation, the immune system forms a large number of immune globulin and rheumatoid factors. Local immune complexes are formed and deposited in joints. When the case is severe, the surface of the bone can be eroded, with morning stiffness, joint pain, swelling, deformation and dysfunction as the main clinical manifestations. The pathogenesis of RA is because the cartilage tissue is damaged, and the absence of immune substances in the synovium of the joint leads to chaos in the metabolism of connective tissue, resulting in antigen variation. This mutated antigen stimulates lymphatic B cells in the synovial membrane of the joint to differentiate into plasma cells, which then produce a large number of mutated antibodies, also known as mutants. This mutation will further stimulate the catalysis and phagocytosis of the lysozyme, causing damage to the synovial cells of the joint. Eventually, RA is induced through a series of autoimmune errors. In order to prevent disease, we should exercise on a regular basis and reduce long-term exposure to humidity. A balanced diet can also help us to prevent disease. Patients with RA should have a positive attitude, follow a balanced diet and exercise regularly; followed in conjunction with other helpful ways, these measures are expected to improve their condition.

The informatisation construction of university continuing education provides convenient conditions for pharmacology course teaching and scientific research. Using network information big data for analysis, we have a preliminary understanding and judgement of the pathogenesis of RA. However, further data mining still needs further research (see Figure 1).
Fig. 1 Big data analysis of age structure of patients with RA. RA, rheumatoid arthritis.

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