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MSNs and MWCNTs Topical Application on Immune Toxicity and Physicochemical Properties

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Research on nanomaterials has become a hot field of materials, which involves physics, chemistry, biology and other disciplines. In this paper, MSNs and MWCNTs were used for the study. By topical route of administration, we study the reaction in mice after application on the immune toxicity of nanomaterials to provide a theoretical basis for the application in pancreatic cancer. With the rapid development of nano-medicine, nano-materials, the body's immune response began to attract attention. The study of nanomaterials in the blood circulation and thus enhancing protein adsorption or suppress the immune response. In recent years, nanomaterials include carbon nanotube, baby ball, fullerene, and emulsions, applicated in immune response and immune therapy. Immune suppression is by inhibiting the proliferation or function of immune-related cells, thereby inhibiting the body's immune response. Immunosuppression is double-edged sword, on the one hand, immune suppression and infection reduces the body's defense ability of cancer cells. On the other hand, it was able to reduce the rejection of organ transplants, but also improve the allergic diseases and autoimmune disease and treatment results. The study found that immunosuppressed mice inhaled carbon nanotubes may activate alveolar cyclooxygenase pathway signal to the spleen.

1. Introduction

Research on nanomaterials has become a hot field of materials, which involves physics, chemistry, biology and other disciplines (Zhang and Li, 2012). Nanomaterials have unique optical, mechanical, electromagnetic and other properties, which have a wide range of applications in all aspects (Streeter, 1998). It has penetrated into our lives, learning all aspects of work, and molecular self-assembly technology in the field of nanotechnology has been widely application (Liu, 2015). In recent years, with the rapid development of nanomedicine, especially in the field of cancer nanotechnology applications in a wide range of cancers, including early diagnosis, molecular imaging and therapy three aspects, optimistic about the future prospects of cancer in clinical applications (Varna, 2012). More and more new nanomaterials are developed and improved (Zhang, 2014).

MSN has many unique properties, high biocompatibility, easy to endocytosis, no significant cytotoxicity (Babu and Zhou, 2015). MSN structured like honeycomb, as a unique "sponge effect", this configuration makes loading mesoporous in small molecule drug or zero leaked ahead until you reach the area only discipline which releases, with beneficial pharmacokinetic characteristics accurate release (Zheng, 2012). MSNs stable and rugged construction, and compared to other polymer drug carrier, baby porous nanoparticles to heat, pH, mechanical stress-induced degradation and hydrolysis more resistant (Cardillo, 2016). Aperture size adjustable, can be adjusted by adjusting the characteristics of chemically loaded in favor of a different drug molecules (Cui and Zhu, 2016).

With the rapid development of nano-medicine, nano-materials and the body's immune response began to attract attention, the study found nanomaterials in the blood circulation and thus enhancing protein adsorption or suppress the immune response. In recent years, nanomaterials include carbon nanotube, baby ball, fullerene, and emulsions. Immune suppression is by inhibiting the proliferation or function of immune-related cells, thereby inhibiting the body's immune response. Immunosuppression is double-edged sword, on the one hand, immune suppression and infection reduces the body's defense ability of cancer cells, but on the other

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hand, was able to reduce the rejection of organ transplants, but also improve the allergic diseases and autoimmune disease and treatment results. After the study found that immunosuppressed mice inhaled carbon nanotubes may activate alveolar cyclooxygenase pathway signal to the spleen.

2. The related theory of physicochemical properties

2.1 AFM characterization techniques

Atomic force microscope by a scanning tunneling microscope (STM) and the inventor of the Stanford University CFQuate Binning and C. Gerber et al (Karimi and Mo, 2016). Invention, which is developed on the basis of the STM, and other microscopy techniques (SEM, TEM) compared to an atomic force microscope has its unique advantages: first, the sample preparation is simple; secondly, AFM is simple, can be operated in the gas phase and liquid phase conditions; again, AFM high resolution, and can be timely to observe the internal structure of the molecule variety (Liu, 2015)).

AFM is a scanning tunneling microscope (STM) based on quantum-mechanical tunneling theory developed on the basis of. It is fixed at one end of the boom, the interaction between the sample and the tip of the other end of the nanoscale morphology and mechanical pattern detecting nanomaterials sample surface. Since the AFM lateral resolution of 0.1nm, the vertical resolution of 0.01nm, so the AFM can obtain accurate information on the mechanical and physical surface morphology of the material. AFM works was shown in Figure 1.

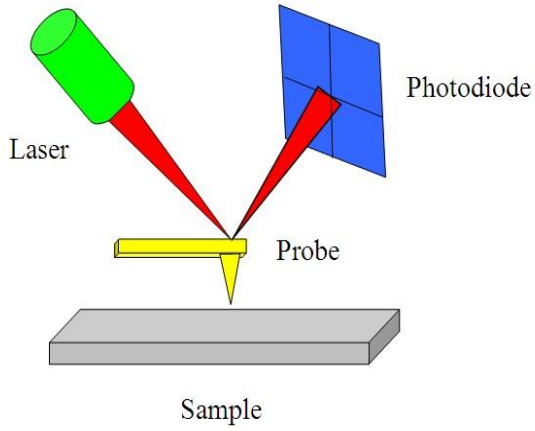

Figure 1: AFM work principle

2.2 AFM topography

Worship dendritic cells to the lymph nodes by the size of the impact of nano-materials, nano-particles of 20-200nm can be draining directly into the lymph node dendritic cells, and large particle size of nanoparticles through cell trafficking to the lymph nodes. Furthermore, the immunogenicity of nanomaterials allows the body to produce specific antibodies, studies suggest that the immunogenicity of nanomaterials are also related to the size of the material _. At present, only three experiments reported nanomaterial-specific antibodies, which are specific antibody binding protein after C60 derivatives can produce polyamide dendrimer binding bovine serum albumin in the body to produce antibodies specific for other experiments using different when nano-materials, such as dendrimers, fullerenes and colloidal gold, but did not find specific immunogenic nanomaterials. Containing polymethyl methacrylate (PAMAM) HIV vaccine nanoparticles in mice, as compared to conventional vaccines containing grinding, which can produce 100 times higher antibody levels. AFM topography image was shown in Figure 2.

The study found single wall carbon nanotubes and multi-walled carbon nanotubes can cause an immune response in mice with ovalbumin-specific bronchial lavage and mediastinal lymph nodes. There are also reports a high degree of exposure to synthetic chemists dendritic polymer semi-finished or finished products who appeared relaxed necrotic dermatitis. However, in order to nanomaterials pharmaceutical formulation able to reduce the allergic reaction, that abraxane (trade name, one of the main active ingredient is a chemotherapeutic drug paclitaxel) in the first generation of non-particle polyoxyethylene ethylene surfactant formulation sesame oil, causing severe hypersensitivity reactions. The need to histamine blockers or steroids while taking; but using 130 nm paclitaxel albumin microspheres entrapped new formula, in advanced breast cancer patients in clinical trials, has been shown to improve allergies, more secure applications.

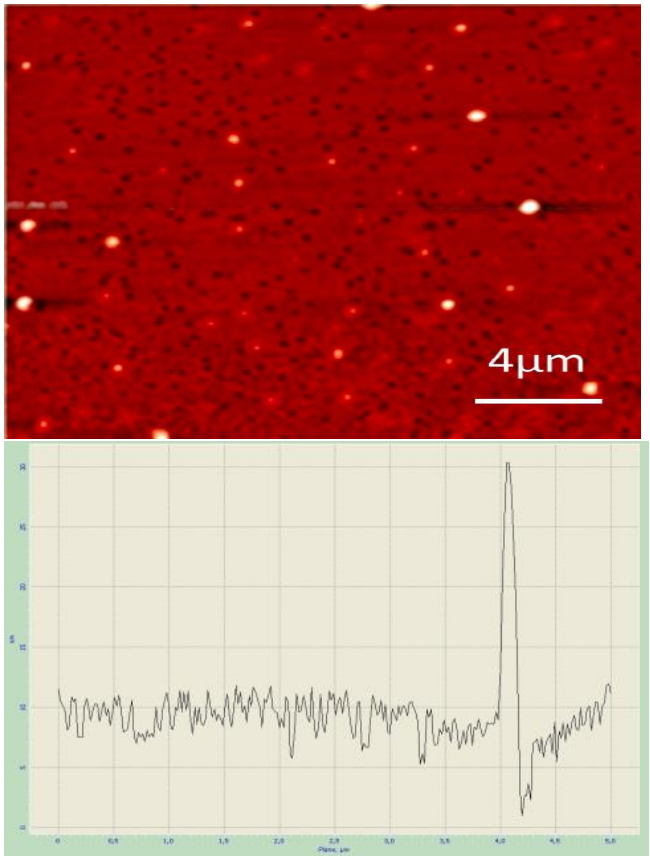

Figure 2: AFM topography image

3. Immunotoxicity study of MSNs and MWCNTs

3.1 Main reagent and material

Polyacrylic acid mesoporous nano baby ball (PAA-g-MSNs): provided by the Institute of Polymer Science, Fudan University
Medical saline: Baxter purchased from China Medical Products Co.
Deionized water: Huashan Hospital Integrative Medicine laboratories
75% ethanol: available from high-tech Co., Ltd. on Haili Kang disinfection
Formalin: Fudan University Huashan Hospital of Xu provided
Blood kit: Sysmex Products
Albumin kit: KHB Products
Alkaline phosphatase kit: KHB Products
Two aminotransferase kit: KHB Products
Aspartate aminotransferase kit: KHB Products
Rats with multiple cytokine detection kit: eBioscience Products
Pity formate buffer base: Model SB0627, Sangon product
Lymphocyte separation medium: Ficoll-PaquePLUS type, GE Healthcare Production
Concanavalin A: Sigma Products
Lipopo Shu ysaccharide: Sigma Products
Tetramethylazodicarboxamide frustration blue (MTT): Sigma Products

3.2 Data collection

(1) General observation: whether there is irritability, drowsiness and other abnormal reactions record mice after administration. Body weight of mice were measured once a week, namely for the first 1,8,16,24,32,40,68,56,64 day, short-term group, only measured three times; the long-term group were measured nine times observed before and after administration changes in body weight of mice.
(2) Bood sampling: selection eyeball blood law, to deter the use of child after removal of the eye, it will take approximately 1ml blood samples were placed in EDTA anticoagulant tubes and EP tube, and mark a good

group number. EDTA anticoagulated blood sample tube and mix well need to shake, for detection of mouse blood; EP tube at 4 °C, 2500rpm centrifugal lOmin, the serum vials into position -8 kept under test.
(3) Dissection: Mice were sacrificed by cervical dislocation, fixed anatomical plate, gradually separated to free the thymus, bilateral popliteal lymph nodes, spleen, liver, heart, lungs and kidneys, the organs removed in physiology rinsed three times with brine, wash away the surface of the blood. Electronic balance organs and lymph nodes measuring weight, fixed in 10% formalin solution.

4. Experiment and results

4.1 Weight change in mice nest lymph nodes

The left and right cerebral fossa lymph nodes compared with the observation group in the short and long-term observation group, the left popliteal lymph node weight and quite right side, no significant difference (P> 0.05) differences.
The left brain fossa lymph nodes between the different groups in the short-term observation group, the left cerebral fossa lymph nodes administration group and the control group considerable weight, the difference was not statistically significant (P> 0.05); in the long-term observation group left brain fossa lymph nodes administration group and the control group considerable weight, the difference was not statistically significant (P> 0.05).
On the right popliteal lymph nodes between the different groups in the short and long-term observation group, the weight of the measurement results on the right cerebral fossa control group, low dose group and high dose groups of lymph nodes is similar, the difference was not statistically significance (P> 0.05) (Figure 3 and Table 1).

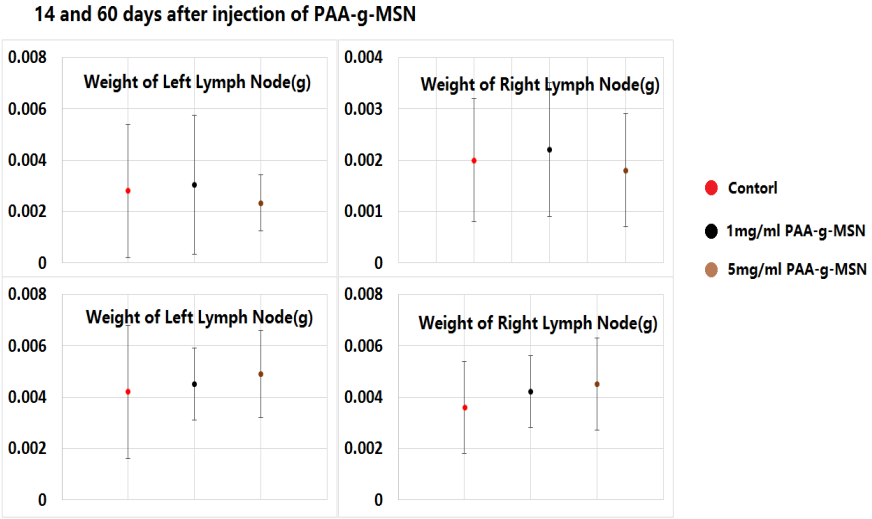

Figure 3: Each lymph nodes weight change in brain nest different times PAA-g-MSN after injection

Table 1: The weight variations of Lymph Node after the injection of PAA-g-MSN

	14 days		60days	
	Weight of Left Lymph Node(g)	Weight of Right Lymph Node(g)	Weight of Left Lymph Node(g)	Weight of Right Lymph Node(g)
Control	0.0028±0.0026	0.002±0.0012	0.0042±0.0026	0.0036±0.0018
1mg/ml PAA-g-MSN	0.003043±0.0027	0.0022±0.0013	0.0045±0.0014	0.0042±0.0014
5mg/ml PAA-g-MSN	0.002329±0.0011	0.0018±0.0011	0.0049±0.0017	0.0045±0.0018

4.2 Effect of hepatic and renal function

The liver and kidney function parameters including total bilirubin (TB), aspartate aminotransferase (ALT), glutamic acid amino transferase (AST), alkaline phosphatase (ALP), total protein (TP), albumin (ALB), urea

nitrogen (BUN) and creatinine (CRE), 14 days of detection were higher than long-term observation group, 60 days in each index declined in varying degrees.

In the short-term observation group, all indicators of liver and kidney function difference between the control group, low-dose administration of high-dose group and the group was not statistically significant (P> 0.05). In the long-term observation group, all indicators of liver and kidney function difference between the control group, the low dose and high-dose administration group was also not statistically significant (P> 0.05) (Table 2).

Table 2: The effect on Hepatorenal function after the injection of PAA-g-MSN

Hepatorenal Function	Hepatorenal function at different dose in different terms					
	14 days			60 days		
	Short term control	1mg/ml PAA-g-MSN	5mg/ml PAA-g-MSN	Long term control	1mg/ml PAA-g-MSN	5mg/ml PAA-g-MSN
TB	2.1±1.57	1.43±0.88	1.75±0.87	1.08±0.54	0.93±0.55	1.83±1.44
ALT	40±7.19	43.75±10.36	36.75±1.8	34.5±2.63	28.25±2.43	30.5±2.53
AST	156±52.73	130.5±34.81	114±13.35	82.5±4.65	69.25±6.02	76.5±4.63
ALP	114.75±27.61	120.75±10.75	129.5±7.14	84.75±6.63	268.5±170.63	139.80±28.23
TP	68.75±11.56	54.5±2.22	59.75±1.11	62±1.15	56±4.32	56±3.65
ALB	46.5±4.03	41±2.04	43±1.08	47±1	42±3.46	39±3.42
BUN	8.46±0.65	13.09±2.35	11.45±1.23	7.18±0.21	5.4±0.59	6.61±0.73
CRE	85.5±51.91	53.5±16.3	42.75±5.5	25±1.29	26.25±3.28	41±11.34

5. Conclusions

In this paper, MSNs and MWCNTs was used for the study, by topical route of administration, study the reaction in mice after application on the immune toxicity of nanomaterials to provide a theoretical basis for the application in pancreatic cancer. With the rapid development of nano-medicine, nano-materials and the body's immune response began to attract attention, the study found nanomaterials in the blood circulation and thus enhancing protein adsorption or suppress the immune response. These nanomaterials include carbon nanotube, baby ball, fullerene, and emulsions. Immune suppression is by inhibiting the proliferation or function of immune-related cells, thereby inhibiting the body's immune response. Immunosuppression is double-edged sword, on the one hand, immune suppression and infection reduces the body's defense ability of cancer cells, but on the other hand, was able to reduce the rejection of organ transplants, but also improve the allergic diseases and autoimmune disease and treatment results.

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