Effects of genetic obesity on rat upper airway muscle and diaphragm contractile properties

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Obstructive sleep apnea is a disorder characterized by intermittent collapse of the pharyngeal upper airway with consequential cessation of ventilation during sleep [1, 2]. There is a close association between obesity and sleep apnea, in that there is a high prevalence of obesity among adults with obstructive sleep apnea and, conversely, a high prevalence of sleep apnea among obese adults [1-4]. Obesity reduces chest wall compliance [5], and in a rat model has recently been found to alter the structural properties and force of some skeletal muscles [6]. The effects of obesity on the upper airway musculature are not known.

Maintenance of pharyngeal patency during breathing is dependent on sufficient activation and contraction of the skeletal muscles which dilate the pharyngeal upper airway. Alterations in structural and/or contractile properties of the pharyngeal muscles have recently been noted in humans and dogs with sleep apnea [7, 8], in humans who snore [9], and in conditions associated with obstructive sleep apnea, including Down's syndrome [10], hypothyroidism [11], diabetes [12], and ageing [14]. Conversely, subjects with primary muscle disease (e.g., muscular dystrophy) have an abnormally high prevalence of obstructive sleep apnea [15, 16]. These data suggest a role for altered intrinsic properties of the pharyngeal musculature in the pathophysiology of obstructive sleep apnea. The present study tested the hypothesis that obesity alters the contractile properties of the pharyngeal dilator musculature. To test this hypothesis, isometric relaxation and force-velocity relationships, fatigue resistance and degree of force potentiation of the sternohyoid and diaphragm muscle were examined in an animal model of genetic obesity, the Zucker rat [17, 18]. Comparisons were made between representatives from muscle groups whose contraction has opposing effects on upper airway patency and which are involved in the pathogenesis and relief of obstructive apneas [1-3, 7], the sternohyoid muscle, which dilates the airway, and the skeletal muscles which dilate the pharyngeal upper airway. Alterations in structural and/or contractile properties of the pharyngeal muscle have recently been noted in humans and dogs with sleep apnea [7, 8], in humans who snore [9], and in conditions associated with obstructive sleep apnea, including Down's syndrome [10], hypothyroidism [11], diabetes [12], and ageing [14].

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Methods

Muscle contractile properties were assessed in vitro. Muscle from nine obese male Zucker rats (mean weight 612 g) was compared with that from nine lean male Zucker rats (mean weight 381 g) of similar age (3-4 months). The animals were anesthetized with intraperitoneal urethane (1-1.5 g/kg). The sternohyoid muscle was removed via a midline cervical incision, and the diaphragm muscle was removed via thoracic and abdominal incisions. Both muscles were removed sequentially in rapid succession from each animal and placed in oxygenated Tyrode solution (see composition below). The muscles were cut into small rectangular strips (width 1-1.5 mm), maintaining the integrity of the bony and/or tendinous origins and insertions. One sternohyoid strip and one diaphragm strip were studied from each animal, except that for one of the obese animals the sternohyoid muscle was damaged during removal and not studied.

The muscle strips were mounted vertically in a double-jacketed bath, whose temperature was maintained at 37°C. The composition of the preparation and bathing solutions was as follows (in mM): 135 NaCl, 5 KCl, 2.5 CaCl₂, 1 MgSO₄, 1 NaH₂PO₄, 15 NaHCO₃, and 11 glucose. The solution was aerated with 5% CO₂-95% O₂, and had its pH adjusted to 7.3-7.4. After a 5 min equilibration period, the muscle strips were stimulated electically (supermaximal voltage, pulse width 1 ms for both muscles) via platinum field electrodes, and muscle length was adjusted to that at which twitch tension was maximal. A high sensitivity isometric transducer (Kent Scientific Corporation, Torrington, CT, USA) was used to measure isometric twitch force. The addition of curare (0.025 mM) to the bath did not alter twitch force in preliminary studies, indicating direct activation of the muscles. For all data reported, sample sizes are nine muscle strips for lean sternohyoid, lean diaphragm and obese diaphragm, and eight muscle strips for obese sternohyoid.

To determine isometric twitch kinetics, muscle strips were stimulated at a frequency of 0.1 Hz. Thereafter, they underwent testing of the force-frequency relationship by stimulation at frequencies of 1, 5, 10, 15, 20, 30, 40, 50, 60, 80 and 100 Hz. Following a brief recovery period, a standard stimulation protocol was used to assess muscle fatigue: 40 Hz pulses lasting 0.33 s were delivered every 1 s for a total of 5 min [8, 13, 14, 19, 20]. Force was quantified by measuring the peak value at any time during the sequence of fatiguing index values were defined as the ratio of peak force at the end of 2 and 5 min of repetitive stimulation to initial force. A high fatigue index, therefore, indicates a greater degree of resistance to fatigue. To assess force potentiation during repetitive stimulation, during the first 40 s of the fatigue protocol each sequence was analysed to determine the presence and extent of augmentation of force relative to that induced during the initial sequence. Force potentiation at 10 s was defined as force after 10 s of stimulation relative to initial force (a negative value indicates force decline rather than force potentiation). The maximum degree of force potentiation was defined as the highest force during any sequence; and expressed relative to force during the initial sequence. In a previous study of the sternohyoid and diaphragm [20], close agreement was found between degree of force potentiation assessed in this manner and force potentiation assessed with staircase and post-tetanic potentiation protocols.

The output from the force transducer was fed via an analogue-to-digital converter to the hard drive of a computer using a standard data acquisition program (Axotape; Axon Instruments, Foster City, CA, USA). Force measurements were made on screen with the use of manually-controlled cursors. Isometric twitch kinetics were quantified by the contraction time (time required to attain maximal twitch force) and the half relaxation time (time required for maximal force to decay by 50%). During the repetitive stimulation protocols, force was normalized to that produced during the first simulation sequence, and expressed as percentage of the initial value. Mean values±SEM were calculated for data from each muscle. Statistical comparisons of data for each muscle between rat strains, and between muscles for a given rat strain, were performed using the unpaired t-test. Statistical comparisons of force-frequency relationships were performed with two-way repeated measures analysis of variance (ANOVA), followed by the Newman-Kuels test when the ANOVA indicated a significant difference. A p-value of less than 0.05 (two-tailed) was considered to indicate statistical significance.

Results

Mean values for the isometric contraction and half relaxation times of the sternohyoid and diaphragm of lean and obese Zucker rats are depicted in figure 1. There were no significant differences between obese and lean animals for sternohyoid contraction time (15.2±6.3 ms vs 14.2±6 ms, respectively) or half relaxation time (13.6±6.5 ms vs 12.5±9.9 ms, respectively), nor did obesity significantly affect diaphragm twitch kinetics. In obese animals, the sternohyoid had faster contraction (p<0.001) and half relaxation times (p<0.001) than the diaphragm, as was the case for lean animals (p<0.001 for both). The twitch-to-tetanic tension ratio was not different for obese compared to lean animals for the sternohyoid.

To assess the rate of fatigue, a standard stimulation protocol was used to assess muscle fatigue: 40 Hz pulses lasting 0.33 s were delivered every 1 s for a total of 5 min [8, 13, 14, 19, 20]. Force was quantified by measuring the peak value at any time during the sequence of fatiguing index values were defined as the ratio of peak force at the end of 2 and 5 min of repetitive stimulation to initial force. A high fatigue index, therefore, indicates a greater degree of resistance to fatigue. To assess force potentiation during repetitive stimulation, during the first 40 s of the fatigue protocol each sequence was analysed to determine the presence and extent of augmentation of force relative to that induced during the initial sequence. Force potentiation at 10 s was defined as force after 10 s of stimulation relative to initial force (a negative value indicates force decline rather than force potentiation). The maximum degree of force potentiation was defined as the highest force during any sequence; and expressed relative to force during the initial sequence. In a previous study of the sternohyoid and diaphragm [20], close agreement was found between degree of force potentiation assessed in this manner and force potentiation assessed with staircase and post-tetanic potentiation protocols.

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Muscle contractile properties were assessed in vitro. Muscle from nine obese male Zucker rats (mean weight 0.213 g) was compared with that from nine lean male Zucker rats (mean weight 0.389 ± 12 g) of similar age (3–4 months). The animals were anesthetized with intraperitoneal pentobarbital (1–1.5 g/kg). The sternothyroid muscle was removed via a midline cervical incision, and the diaphragm muscle was removed via thoracic and abdominal incisions. Both muscles were removed sequentially in rapid succession from each animal and placed in oxygenated (95% O2, 5% CO2) Krebs solution (composition below). The muscles were cut into small rectangular strips (width 1–1.5 mm), maintaining the integrity of the bony and/or tendinous origins and insertions. One diaphragm strip and one sternothyroid strip were studied from each animal, except that for one of the obese animals the sternothyroid muscle was damaged during removal and not studied. The muscle strips were mounted vertically in a double-jacketed bath, whose temperature was maintained at 37°C. The composition of the preparation and bathing solutions was as follows (in mM): 115 NaCl, 5 KCl, 2.5 CaCl2, 1 MgSO4, 1 NaH2PO4, 15 NaHCO3, and 11 glucose. The solution was aerated with 5% CO2–95% O2, and had its pH adjusted to 7.3–7.4. After a 5 min equilibration period, the muscle strips were stimulated electrically (supermaximal voltage, pulse width 1 ms for both muscles) via platinum field electrodes, and muscle length was adjusted to that at which twitch tension was maximal. A high sensitivity isotonic transducer (Kendall Scientific Corporation, Pinole, CA, USA) was used to measure isotonic twitch force. The addition of curare (0.025 mM) to the bath did not alter twitch force in preliminary studies, indicating direct activation of the muscles. For all data reported, sample sizes are nine muscle strips for lean sternothyroid, lean diaphragm, and obese diaphragm, and eight muscle strips for obese sternothyroid. To determine isotonic twitch kinematics, muscle strips were stimulated at a frequency of 0.1 Hz. Thereafter, they underwent testing of the force-frequency relationship by stimulation at frequencies of 1, 5, 10, 15, 20, 30, 40, 50, 60, 80, and 100 Hz. Following a brief recovery period, a standard stimulation protocol was used to assess muscle fatigue: 40 Hz pulses lasting 0.33 s were delivered every 1 s for a total of 5 s [8, 13, 14, 15, 19]. Force was quantified by measuring the peak value at any time during the sequence of fatigue indices were defined as the ratio of peak force at the end of 2 and 5 min of repetitive stimulation to initial force. A high fatigue index, therefore, indicates a greater degree of resistance to fatigue. To assess force potentiation during repetitive stimulation, during the first 40 s of the fatigue protocol each sequence was analyzed to determine the presence and extent of augmentation of force relative to that induced during the initial sequence. Force potentiation at 10 s of stimulation was defined as the highest force achieved after 10 s of stimulation relative to initial force (a negative value indicates force decline rather than force potentiation). The maximum degree of force potentiation was defined as the highest force during any sequence; and expressed relative to force during the initial sequence. In a previous study of the sternothyroid and diaphragm [20], close agreement was found between degree of fatiguing potentiation assessed in this manner and force potentiation assessed with staircase and post-tetanic potentiation protocols. The output of the force transducer was fed via an analog-to-digital converter to the hard drive of a computer running a standard data acquisition program (Axotape, Axon Instruments, Foster City, CA, USA). Force measurements were made on screen with the use of manually controlled cursors. Isometric twitch kinematics were quantified by the contraction time (time required to attain maximal twitch force) and the half relaxation time (time required for muscle force to decay by 50%). During the repetitive stimulation protocols, force was normalized to that produced during the first stimulation sequence, and expressed as a percentage of the initial force. Mean values±SEM were calculated for data from each muscle. Statistical comparisons of data for each muscle between rat strains, and between muscles for a given rat strain, were performed using the unpaired t-test. Statistical comparisons of force-frequency relationships were performed with two-way repeated measures analysis of variance (ANOVA), followed by the Newman-Kuels test when the ANOVA indicated a significant difference. A p-value of less than 0.05 (two-tailed) was considered to indicate statistical significance.

Results

Mean values for the isotonic contraction and half relaxation times of the sternothyroid and diaphragm of lean and obese Zucker rats are depicted in figure 1. There were no significant differences between obese and lean animals for sternothyroid contraction time (15.2±0.3 vs 14.2±0.6 ms, respectively) or half-relaxation time (13.6±0.5 vs 12.5±0.9 ms, respectively), nor did obesity significantly affect diaphragm twitch kinetics. In obese animals, the sternothyroid had faster contraction (p<0.001) and half-relaxation times (p<0.001) than the diaphragm, as was the case for the control group (p<0.001). The twitch-to-tetanic tension ratio was not different for obese compared to lean animals for the sternothyroid muscle (0.22±0.02 vs 0.24±0.04, respectively), but was significantly lower for obese than lean animals for the diaphragm muscle (0.25±0.01 vs 0.29±0.02, respectively) (p<0.05). In obese animals, there was no significant difference between the two muscles in twitch-to-tetanic tension ratios, in contrast to lean animals in which differences were found (p<0.05). Obesity did not significantly alter the force-frequency relationship either for the sternothyroid or diaphragm muscle (figure 2). In obese animals, there was no significant difference between the two muscles in the force-frequency relationship, whereas in lean animals force-frequency relationship of the sternothyroid was located significantly to the right of that of the diaphragm (p<0.02). Values for the 2 and 5 min fatigue indices during repetitive 40 Hz stimulation are shown in figure 3. For the sternothyroid muscle, there were no significant differences between obese and lean rats in the degree to which force declined following 2 and 5 min of repetitive stimulation (2 min fatigue index 0.20±0.03 vs 0.24±0.02, respectively; 5 min fatigue index 0.13±0.02 vs 0.11±0.01, respectively). Furthermore, obesity did not affect diaphragm fatigue resistance significantly. In obese animals, the diaphragm had significantly higher 2 and 5 min fatigue indices than the sternothyroid muscle (0.20±0.02 and 0.01, respectively), as was the case for lean animals (0.001 and 0.001, respectively). During repetitive stimulation, force of the sternothyroid muscle initially increased prior to a rapid rate of decline (fig. 4a). There were no significant differences between obese and lean animals in the degree to which sternothyroid muscle force changed at specific time intervals (fig. 4a) or in the maximal force at any point in time (52±11 vs 74±20%, increase, respectively) (fig. 4b). The diaphragm...
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exhibited a significantly shorter- and shorter-lived force increase, which was also affected by obesity. In obese animals, the maximal force was significantly greater for the sternohyoid than for the diaphragm, with a delay of 45-70 ms in the onset of contraction. In lean animals, there were some trends which if in opposite directions for the two muscles could potentially affect the relationship of these muscles over time. Figure 5 examines this relationship directly, and indicates that obesity produced only a small change in the relationship of the sternohyoid to the diaphragm force, which was limited to the early portion of repetitive stimulation.

Discussion

The sternohyoid muscle is one of many pharyngeal muscles which dilates the upper airway [21, 22]. Considerable information is available about its structural and contractile properties in various species [7, 11, 13, 19, 20, 23]. Alterations have been found in this muscle, but not in the genioglossus muscle, in dogs with obesity. Whether obese animals differ from lean animals in phrenic and/or hypoglossal motoneuronal firing rates during breathing is not known, so the impact of altered relationships between the phrenic and hypoglossal force relationships in the intact animal is difficult to predict.

The paucity of changes in contractile properties of the sternohyoid muscle with obesity contrasts with the effects of development and ageing, both of which significantly affect sternohyoid fatigue resistance. The effects of ageing were examined in Fischer 344 rats: compared to young muscle (3-4 month old rats), the muscle (20-21 months old) had impaired fatigue resistance (the 2 min fatigue index decreased from 0.18 to 0.10, and the 5 min fatigue index decreased from 0.10 to 0.03) despite no change in isometric twitch kinetics [14]. In that study, the old animals weighed more than the young animals (~770 g vs ~300 g, respectively). The present data indicate no effects of obesity on sternohyoid muscle fatigue resistance, consistent with previous work [13]. Whether obesity affects fatigue resistance of young muscle, and whether these effects are unique to older muscle is currently unknown.

The effects of ageing were examined in Fischer 344 rats: compared to young muscle (3-4 month old rats), the muscle (20-21 months old) had impaired fatigue resistance (the 2 min fatigue index decreased from 0.52 to 0.36 with development) but no differences in isometric twitch kinetics, twitch-to-tetanic ratio, twitch-to-tetanic tension ratio, or force-frequency relationship during the early part of the fatiguing stimulation. The only difference between the two muscles was regarded to the effect of obesity is that Farkas et al. [6] found that obesity significantly prolonged diaphragm contraction time (from 21.2 to 25.1 ms), whereas in the present study there was a trend to increased contraction time (from 22.7 to 23.6 ms), which was not statistically significant. The reason for the small difference between studies is not methodology for determining contraction time is highly standardized, so that differences in technique between studies are an unlikely explanation. On the other hand, Farkas et al. [6] found that young animals with 3-4 month old rats were used in the present study, so differences in age or gender between studies are a more likely explanation.

In the present study, it was found that both for obese and lean animals the sternohyoid and diaphragm demonstrated a lower degree of force potentiation (maximum increases of 74 and 52% in lean and obese animals, respectively) whereas the diaphragm showed greater force potentiation (maximum increases of 2% and 5% in lean and obese animals, respectively) during the early portion of the stimulation. Whether these contractile properties of the diaphragm in lean and obese rats did not specifically address force potentiation, but investigating young (3-4 month old) muscle. The effects of obesity on force potentiation were found for the sternohyoid muscle, whereas the diaphragm muscle was not significantly affected by obesity. The findings of this study are consistent with previous study by Kruh et al. [25] that obese animals had significantly reduced force potentiation, indicating that obesity impaired the force potentiation of the sternohyoid muscle.
exhibited a pronounced short and shorter-lived force increase, which was also significantly affected by obesity. In obese animals, the maximal force was significantly greater for the sternohyoid muscle (p < 0.001), as was the case for lean animals (p<0.005). Although obesity did not significantly affect force potentiation or fatigability of the diaphragm, there were some trends which if in opposite directions for the two muscles could potentially affect the relationship between obesity and muscle function over time. Figure 5 examines this relationship directly, and indicates that obesity produced only a small change in the intrinsic force potentiation of the diaphragm, which was limited to the early portion of repetitive stimulation.

The sternohyoid muscle is one of many pharyngeal muscles which dilates the upper airway [21, 22]. Considerable information is available on the structural and contractile properties in various species [7, 11, 13, 19, 20, 23]. Alterations have been found in this muscle, but not in the genioglossus muscle in a dog model of sleep apnoea: a higher proportion of fast fibres; an increased proportion of morphologically abnormal fibres, consistent with previous or ongoing injury; and a greater connective tissue content, consistent with fibrosis [7]. The sternohyoid muscle was the primary focus for current study based on the above considerations, as well as the fact that it is easier to distinguish from surrounding tissues and, hence, easier to dissect from the genioglossus and especially the genioglossus muscles, minimizing the chance of tissue damage. Previous studies have examined the contractile properties of the sternohyoid muscle in the adult rat, the sternohyoid, sternothyroid, genioglossus, and geniobuccal muscles in the adult cat, and the muscles uvulae in adult humans [8, 14, 19, 20, 24, 25]. These muscles generally have fast isotonic contraction and relaxation and do not possess slow twitch-to-tetanic tension ratios, a more rightward force-frequency relation than the diaphragm, a high degree of force potentiation, and variable resistance to fatigue (which differs among muscles and among species). The present data for the sternohyoid muscle in lean Zucker rats are consistent with previous data in normal Sprague-Dawley and Fischer 344 rats [14, 20]. The present study found that genetic obesity in rats had no significant effects on the following physiological properties of the sternohyoid muscle: isotonic twitch tension, twitch-to-tetanic tension ratio, force-frequency relationship, force potentiation and fatigue resistance. Furthermore, the relationship between the contractile properties of the sternohyoid and the diaphragm was not altered by obesity, with the following exceptions: in lean animals the sternohyoid twitch-to-tetanic force ratio was lower than in animals of either genotype, but the effect of the right-hand side of that of the diaphragm on the other muscles) showed no significant effect. In lean animals these two properties did not differ between the sternohyoid and the diaphragm. The relationships between obesity and lean animals will impact the transduction of motoneuronal firing rates into muscle force, specifically making the transduction between the two muscles more similar in obese animals than lean animals. Observations of fatigue responses to hypoxia (21%), but no alterations in resting or ventilatory responses to hypoxia, compared to lean animals. Whether obese (by lean) animals in previous studies demonstrated considerable fatigability (maximum increases of 74% and 52% in lean and obese animals, respectively) whereas the diaphragm demonstrated considerably higher fatigue (maximum increases of 2% and 5% in lean and obese animals, respectively) during the early portion of the stimulation. The present data are consistent with our previous study in Sprague-Dawley rats, in which substantially greater force potentiation was not noted for the sternohyoid muscle than the diaphragm (maximum force increases of 33% and 35% in lean and obese animals, respectively) during the early portion of the stimulation. The degree of force potentiation noted for the diaphragm in the present study is within the range reported previously. The present study argues against alterations in the contractile properties of the diaphragm in lean and obese rats did not specifically address force potentiation, but instead evaluated effects on the pharyngeal muscles and found no differences in contractile and fatigue resistance, or tetanic tension, in subjects with obesity compared to lean rats. The present study did not specifically address force potentiation, whereas in rats obesity has no physiological effects on pharyngeal muscles, so that the animals do not develop sleep apnoea. Thus, it is possible that obesity has a primary effect on pharyngeal muscles in humans which leads to sleep apnoea. In rats, in which there are no physiological effects on pharyngeal muscles, so that the animals do not not develop sleep apnoea. Studies of pharyngeal muscles in obese rodents and awake and asleep apnoea are needed to better address these issues.

References
Pseudomonas aeruginosa adherence to remodelling respiratory epithelial cells

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ABSTRACT: Pseudomonas aeruginosa is an opportunistic organism, which frequently colonizes the respiratory tract of patients with impaired host defense. In cystic fibrosis (CF) patients, this pathogen causes a progressive destructive bronchitis and bronchiolitis and is responsible for high mortality.

Normal respiratory epithelium is protected against bacteria via mucus and mucociliary clearance. Alteration of mucociliary clearance and of glycosylation of mucins in CF facilitates the access of bacteria to the underlying airway epithelial cells. Inactive respiratory epithelium does not bind P. aeruginosa, whereas injured respiratory epithelium is highly susceptible to P. aeruginosa adherence. We found that the high affinity of respiratory epithelium, from CF and non-CF sources, for P. aeruginosa, during the wound repair process is related to the apical expression of integrin family subunits (e.g., vimentin), to P. aeruginosa is time-dependent, and to transient apical expression of α-v integrin, at the surface of repairing respiratory epithelial cells. CF respiratory epithelial cells apically express more α-v integrin residues with relation to an increased affinity for P. aeruginosa than non-CF cells. High epithelial damage followed by repair represents a major cause of P. aeruginosa adherence to airway epithelium in cystic fibrosis. However, P. aeruginosa adherence and colonization are not restricted to cystic fibrosis disease and P. aeruginosa pneumonia may also occur in severely immunocompromised patients, suggesting that epithelial injury and decreased host resistance favour the colonization of the airways by P. aeruginosa.

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Among various bacteria able to colonize airways, Pseudomonas aeruginosa is an opportunistic microorganism often recovered in the airways of patients with an impairment in their host defense. Among the populations having a high risk to develop P. aeruginosa pneumonia, patients admitted to intensive care units with respiratory assistance represent the most exposed population. Another exposed population includes patients under-going chemotherapy following cancer. The cystic fibrosis (CF) population represents a group for which P. aeruginosa infection is particularly important. Although P. aeruginosa has been associated with CF disease for a long time, it is of interest that recent reports from the National Nosocomial Infections Surveillance System in the United States demonstrated that P. aeruginosa is the most frequent pathogen causing nosocomial pneumonia [1]. This clearly demonstrates that cystic fibrosis transmembrane conductance regulator (CFTR) mutation leading to CF disease does not represent the only factor which allows P. aeruginosa to colonize airways.

In CF, P. aeruginosa infection of patients generally appears at the age of 10–14 yrs; other pathogens such as Streptococcus pneumoniae, Haemophilus influenzae and Staphylococcus aureus, appear earlier. After this age, nearly 98% of the CF population is colonized by P. aeruginosa. The eradication of P. aeruginosa by antimicrobial therapy is rarely possible, leading to a progressive destructive bronchitis, and bronchiolitis with ultimate respiratory failure and severe deterioration of the patient’s clinical status. Due to the impairment of mucociliary transport and to an increased production of P. aeruginosa and neutrophil elastases combined with other bacterial exoproducts, the mucous barrier and the respiratory epithelium may be severely damaged and remodelled. These particular environmental conditions in CF may expose neutrophils for P. aeruginosa adhesion. The initial step of bacterial infection, preceding chronic colonization is the adherence of the bacteria to the epithelial cells. In normal conditions, the epithelial cells are protected by the airway mucus. In contrast, during impairment of host defense, an easier access of bacteria to epithelial cells could be achieved, particularly during the process of wound repair. Therefore, the limitation or the prevention of bacterial adherence are probably the most important means to prevent colonization by P. aeruginosa in exposed populations.

P. aeruginosa binding to respiratory mucins

In normal conditions, the surface epithelium is covered by a thin mucous layer, which functions as a filtration.